## **PCT**

# WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7:
C12N 15/00, C07K 14/00

A1

(11) International Publication Number: WO 00/37630

(43) International Publication Date: 29 June 2000 (29.06.00)

(21) International Application Number: PCT/US99/31005

(22) International Filing Date: 22 December 1999 (22.12.99)

(30) Priority Data: 09/220,876 23 December 1998 (23.12.98) US

(71) Applicant: GENETICS INSTITUTE, INC: [US/US]; 87 CambridgePark Drive, Cambridge, MA 02140 (US).

(72) Inventors: JACOBS, Kenneth; 151 Beaumont Avenue, Newton, MA 02160 (US). MCCOY, John, M.; 56 Howard Street, Reading, MA 01867 (US). LAVALLIE, Edward, R.; 113 Ann Lee Road, Harvard, MA 01451 (US). COLLINS-RACIE, Lisa, A.; 124 School Street, Acton, MA 01720 (US). EVANS, Cheryl; 18801 Bent Willow Circle, Germantown, MD 20874 (US). MERBERG, David; 2 Orchard Drive, Acton, MA 01720 (US). TREACY, Maurice; 12 Foxrock Court, Dublin 18 (IE). BOWMAN, Michael, R.; 50 Aldrich Road, Canton, MA 02021 (US).

(74) Agent: MANDRAGOURAS, Amy, E.; Lahive & Cockfield, LLP, 28 State Street, Boston, MA 02109 (US).

(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

#### **Published**

With international search report.

Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: SECRETED PROTEINS

(57) Abstract

Novel proteins are disclosed.

## FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

					*		
AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Fintand	LT	Lithuania	SK	Slovakia
ΑT	Austria	FR	France	LU	Luxembourg	SN	Senegal
ΑU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
ΑZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	· TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav	· TM	Turkmenistan
BF	Burkina Faso	GR	Greece		Republic of Macedonia	TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali .	TT	Trinidad and Tobago
BJ	Benin	ΙE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL.	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi `	US	United States of America
CA	Canada	ΙT	Italy	MX	Mexico	· UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland .	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's	NZ	New Zealand		•
CM	Cameroon		Republic of Korea	PL	Poland		
· CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	Li	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		•
EE	Estonia	LR	Liberia	SG	Singapore		•

# SECRETED PROTEINS

5		This application is a continuation-in-part of the following applications:
	(1)	Ser. No. 08/634,325, filed April 18, 1996;
	(2)	Ser. No. 08/783,520, filed January 13, 1997, which is a
		continuation-in-part of application Ser. No. 08/634,325, filed April 18,
10		1996;
	(3)	Ser. No. 08/885,610, filed June 30, 1997, which is a continuation-in-part
		of application Ser. No. 08/634,325, filed April 18, 1996;
	(4)	Ser. No. 08/943,861, filed October 3, 1997, which is a continuation of
		application Ser. No. 60/080,227 (converted to a provisional application
15		from non-provisional application 08/725,885), filed October 4, 1996;
	(5)	Ser. No. 08/943,862, filed October 3, 1997, which is a continuation of
		application Ser. No. 60/093,043 (converted to a provisional application
		from non-provisional application 08/726,257), filed October 4, 1996;
	(6)	Ser. No. 08/960,024, filed October 29, 1997, which is a
20		continuation-in-part of application Ser. No. 60/077,176 (converted to a
		provisional application from non-provisional application 08/742,973),
		filed November 1, 1996; and
	(7)	Ser. No. 09/137,226, filed August 20, 1998, which is a
	•	continuation-in-part of application Ser. No. 60/092,114 (converted to a
25		provisional application from non-provisional application 08/916,041),
	·	filed August 21, 1997;

all of which are incorporated by reference herein.

#### FIELD OF THE INVENTION

The present invention provides novel proteins , along with therapeutic, diagnostic and research utilities for these proteins.

#### BACKGROUND OF THE INVENTION

10 Technology aimed at the discovery of protein factors (including e.g., cytokines, such as lymphokines, interferons, CSFs and interleukins) has matured rapidly over the past decade. The now routine hybridization cloning and expression cloning techniques clone novel polynucleotides "directly" in the sense that they rely on information directly related to the discovered protein (i.e., partial DNA/amino acid 15 sequence of the protein in the case of hybridization cloning; activity of the protein in the case of expression cloning). More recent "indirect" cloning techniques such as signal sequence cloning, which isolates DNA sequences based on the presence of a now well-recognized secretory leader sequence motif, as well as various PCR-based or low. stringency hybridization cloning techniques, have advanced the state of the art by making available large numbers of DNA/amino acid sequences for proteins that are known to have biological activity by virtue of their secreted nature in the case of leader sequence cloning, or by virtue of the cell or tissue source in the case of PCR-based techniques. It is to these proteins that the present invention is directed.

10

15

20

25

#### SUMMARY OF THE INVENTION

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

- 5 (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:1;
  - (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:1 from nucleotide 19 to nucleotide 561;
  - (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AK296\_1i deposited under accession number ATCC 98026;
    - (d) a polynucleotide encoding the full-length protein encoded
       by the cDNA insert of clone AK296\_1i deposited under accession number ATCC
       98026;
  - (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AK296\_1i deposited under accession number ATCC 98026;
    - (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AK296\_1i deposited under accession number ATCC 98026;
    - (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:2;
    - (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:2 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:2;
    - (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and
    - (j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:1 from nucleotide 19 to nucleotide 561; the nucleotide sequence of the full-length protein coding sequence of clone AK296\_1i deposited under accession number ATCC 98026; or the nucleotide sequence of a mature protein coding sequence of clone AK296\_1i deposited under accession number ATCC 98026. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert

of clone AK296\_1i deposited under accession number ATCC 98026. In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:2 from amino acid 3 to amino acid 181. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:2 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:2, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:2 having biological activity, the fragment comprising the amino acid sequence from amino acid 85 to amino acid 94 of SEQ ID NO:2.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

10

- (a) the amino acid sequence of SEQ ID NO:2;
- 15 (b) the amino acid sequence of SEQ ID NO:2 from amino acid 3 to amino acid 181;
  - (c) fragments of the amino acid sequence of SEQ ID NO:2, each fragment comprising eight consecutive amino acids of SEQ ID NO:2; and
- (d) the amino acid sequence encoded by the cDNA insert of clone AK296\_1i deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:2 or the amino acid sequence of SEQ ID NO:2 from amino acid 3 to amino acid 181. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:2 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:2, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:2, the fragment comprising the amino acid sequence from amino acid 85 to amino acid 94 of SEQ ID NO:2.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:3;

5

10

15

20

30

(b) a polynucleotide comprising the nucleotide sequence of SEQID NO:3 from nucleotide 123 to nucleotide 1457;

- (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AK533\_1i deposited under accession number ATCC 98026;
- (d) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AK533\_1i deposited under accession number ATCC 98026;
- (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AK533\_1i deposited under accession number ATCC 98026;
  - (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AK533\_1i deposited under accession number ATCC 98026;
  - (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:4;
  - (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:4 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:4;
  - (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and
    - (j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:3 from nucleotide 123 to nucleotide 1457; the nucleotide sequence of the full-length protein coding sequence of clone AK533\_1i deposited under accession number ATCC 98026; or the nucleotide sequence of a mature protein coding sequence of clone AK533\_1i deposited under accession number ATCC 98026. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AK533\_1i deposited under accession number ATCC 98026.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:4;
- (b) fragments of the amino acid sequence of SEQ ID NO:4, each

fragment comprising eight consecutive amino acids of SEQ ID NO:4; and

(c) the amino acid sequence encoded by the cDNA insert of clone AK533\_1i deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:4. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:4 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:4, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:4, the fragment comprising the amino acid sequence from amino acid 217 to amino acid 226 of SEQ ID NO:4.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

15 (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:5;

: 20

25

- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:5 from nucleotide 258 to nucleotide 392;
- (c) a polynucleotide comprising the nucleotide sequence of SEQID NO:5 from nucleotide 330 to nucleotide 392;
  - (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AK583\_1i deposited under accession number ATCC 98026;
  - (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AK583\_1i deposited under accession number ATCC 98026;
  - (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AK583\_1i deposited under accession number ATCC 98026:
  - (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AK583\_1i deposited under accession number ATCC 98026;
  - (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:6;
    - (i) a polynucleotide encoding a protein comprising a fragment

5

10

15

20

of the amino acid sequence of SEQ ID NO:6 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:6;

- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:5 from nucleotide 258 to nucleotide 392; the nucleotide sequence of SEQ ID NO:5 from nucleotide 330 to nucleotide 392; the nucleotide sequence of the full-length protein coding sequence of clone AK583\_1i deposited under accession number ATCC 98026; or the nucleotide sequence of a mature protein coding sequence of clone AK583\_1i deposited under accession number ATCC 98026. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AK583\_1i deposited under accession number ATCC 98026.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:6;
- (b) fragments of the amino acid sequence of SEQ ID NO:6, each fragment comprising eight consecutive amino acids of SEQ ID NO:6; and
- (c) the amino acid sequence encoded by the cDNA insert of clone AK583\_1i deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:6. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:6 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:6, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:6, the fragment comprising the amino acid sequence from amino acid 17 to amino acid 26 of SEQ ID NO:6.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ

5

10

15

20

25

ID NO:7;

- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:7 from nucleotide 6 to nucleotide 1424;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:7 from nucleotide 78 to nucleotide 1424;
  - (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AM282\_1i deposited under accession number ATCC 98026;
- (e) a polynucleotide encoding the full-length protein encoded
   by the cDNA insert of clone AM282\_1i deposited under accession number ATCC
   98026;
  - (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AM282\_1i deposited under accession number ATCC 98026;
  - (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AM282\_1i deposited under accession number ATCC 98026;
  - (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:8;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:8 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:8;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:7 from nucleotide 6 to nucleotide 1424; the nucleotide sequence of SEQ ID NO:7 from nucleotide 78 to nucleotide 1424; the nucleotide sequence of the full-length protein coding sequence of clone AM282\_1i deposited under accession number ATCC 98026; or the nucleotide sequence of a mature protein coding sequence of clone AM282\_1i deposited under accession number ATCC 98026. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AM282\_1i deposited under accession number ATCC 98026. In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence

of SEQ ID NO:8 from amino acid 1 to amino acid 91. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:8 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:8, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:8 having biological activity, the fragment comprising the amino acid sequence from amino acid 231 to amino acid 240 of SEQ ID NO:8.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

15

- (a) the amino acid sequence of SEQ ID NO:8;
- (b) the amino acid sequence of SEQ ID NO:8 from amino acid 1 to amino acid 91;
- (c) fragments of the amino acid sequence of SEQ ID NO:8, each fragment comprising eight consecutive amino acids of SEQ ID NO:8; and
- (d) the amino acid sequence encoded by the cDNA insert of clone AM282\_1i deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:8 or the amino acid sequence of SEQ ID NO:8 from amino acid 1 to amino acid 91. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:8 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:8, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:8, the fragment comprising the amino acid sequence from amino acid 231 to amino acid 240 of SEQ ID NO:8.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

- $\hbox{ (a)} \qquad \hbox{a polynucleotide comprising the nucleotide sequence of SEQ} \\ \hbox{ID NO:9;} \\$
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:9 from nucleotide 87 to nucleotide 458;

5

10

15

20

- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:9 from nucleotide 378 to nucleotide 458;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AM340\_1i deposited under accession number ATCC 98026;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AM340\_1i deposited under accession number ATCC 98026:
- a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AM340\_1i deposited under accession number ATCC 98026;
  - (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AM340\_1i deposited under accession number ATCC 98026;
  - (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:10;
  - (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:10 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:10;
  - (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and
    - (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:9 from nucleotide 87 to nucleotide 458; the nucleotide sequence of SEQ ID NO:9 from nucleotide 378 to nucleotide 458; the nucleotide sequence of the full-length protein coding sequence of clone AM340\_1i deposited under accession number ATCC 98026; or the nucleotide sequence of a mature protein coding sequence of clone AM340\_1i deposited under accession number ATCC 98026. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AM340\_1i deposited under accession number ATCC 98026.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:10;

(b) fragments of the amino acid sequence of SEQ ID NO:10, each fragment comprising eight consecutive amino acids of SEQ ID NO:10; and

- (c) the amino acid sequence encoded by the cDNA insert of clone AM340\_1i deposited under accession number ATCC 98026;
- the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:10. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:10 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:10, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:10, the fragment comprising the amino acid sequence from amino acid 57 to amino acid 66 of SEQ ID NO:10.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

15

20

25

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:11;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:11 from nucleotide 17 to nucleotide 685;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:11 from nucleotide 86 to nucleotide 685;
  - (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AM610\_1i deposited under accession number ATCC 98026;
- (e) a polynucleotide encoding the full-length protein encoded
   by the cDNA insert of clone AM610\_1i deposited under accession number ATCC
   98026;
  - (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AM610\_1i deposited under accession number ATCC 98026;
  - (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AM610\_1i deposited under accession number ATCC 98026;
  - (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:12;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:12 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:12;

- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:11 from nucleotide 17 to nucleotide 685; the nucleotide sequence of SEQ ID NO:11 from nucleotide 86 to nucleotide 685; the nucleotide sequence of the full-length protein coding sequence of clone AM610\_1i deposited under accession number ATCC 98026; or the nucleotide sequence of a mature protein coding sequence of clone AM610\_1i deposited under accession number ATCC 98026. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AM610\_1i deposited under accession number ATCC 98026.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

20

- (a) the amino acid sequence of SEQ ID NO:12;
- (b) fragments of the amino acid sequence of SEQ ID NO:12,each fragment comprising eight consecutive amino acids of SEQ ID NO:12; and
- (c) the amino acid sequence encoded by the cDNA insert of clone AM610\_1i deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:12. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:12 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:12, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:12, the fragment comprising the amino acid sequence from amino acid 106 to amino acid 115 of SEQ ID NO:12.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

5

10

15

20 -

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:13;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:13 from nucleotide 70 to nucleotide 504;
- (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AP162\_1i deposited under accession number ATCC 98026;
- (d) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AP162\_1i deposited under accession number ATCC 98026;
- (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AP162\_1i deposited under accession number ATCC 98026;
- (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AP162\_1i deposited under accession number ATCC 98026;
- (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:14;
- (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:14 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:14;
- (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and
- (j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.
- Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:13 from nucleotide 70 to nucleotide 504; the nucleotide sequence of the full-length protein coding sequence of clone AP162\_1i deposited under accession number ATCC 98026; or the nucleotide sequence of a mature protein coding sequence of clone AP162\_1i deposited under accession number ATCC 98026. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AP162\_1i deposited under accession number ATCC 98026. In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:14 from amino acid 42 to amino acid 61. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a

fragment of the amino acid sequence of SEQ ID NO:14 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:14, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:14 having biological activity, the fragment comprising the amino acid sequence from amino acid 67 to amino acid 76 of SEQ ID NO:14.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- 10 (a) the amino acid sequence of SEQ ID NO:14;
  - (b) the amino acid sequence of SEQ ID NO:14 from amino acid 42 to amino acid 61;
  - (c) fragments of the amino acid sequence of SEQ ID NO:14, each fragment comprising eight consecutive amino acids of SEQ ID NO:14; and
- (d) the amino acid sequence encoded by the cDNA insert of clone AP162\_1i deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:14 or the amino acid sequence of SEQ ID NO:14 from amino acid 42 to amino acid 61. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:14 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:14, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:14, the fragment comprising the amino acid sequence from amino acid 67 to amino acid 76 of SEQ ID NO:14.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

25

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:16:
  - (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:16 from nucleotide 77 to nucleotide 694;
  - (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AR260\_1i deposited under accession

number ATCC 98026;

5

15

30

- (d) a polynucleotide encoding the full-length protein encoded
   by the cDNA insert of clone AR260\_1i deposited under accession number ATCC
   98026;
- (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AR260\_1i deposited under accession number ATCC 98026;
- (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AR260\_1i deposited under accession number ATCC 98026;
- 10 (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:17;
  - (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:17 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:17;
  - (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and
  - (j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:16 from nucleotide 77 to nucleotide 694; the nucleotide sequence of the full-length protein coding sequence of clone AR260\_1i deposited under accession number ATCC 98026; or the nucleotide sequence of a mature protein coding sequence of clone AR260\_1i deposited under accession number ATCC 98026. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AR260\_1i deposited under accession number ATCC 98026.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:17;
- (b) fragments of the amino acid sequence of SEQ ID NO:17, each fragment comprising eight consecutive amino acids of SEQ ID NO:17; and
- (c) the amino acid sequence encoded by the cDNA insert of clone AR260\_1i deposited under accession number ATCC 98026; the protein being substantially free from other mammalian proteins. Preferably such

protein comprises the amino acid sequence of SEQ ID NO:17. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:17 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:17, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:17, the fragment comprising the amino acid sequence from amino acid 98 to amino acid 107 of SEQ ID NO:17.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

15

20

25

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:18;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:18 from nucleotide 23 to nucleotide 676;
- (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AS32\_1i deposited under accession number ATCC 98026;
- (d) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AS32\_1i deposited under accession number ATCC 98026;
- (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AS32\_1i deposited under accession number ATCC 98026;
- (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AS32\_1i deposited under accession number ATCC 98026;
- (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:19;
- (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:19 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:19;
- (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and
- (j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

PCT/US99/31005 WO 00/37630

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:18 from nucleotide 23 to nucleotide 676; the nucleotide sequence of the full-length protein coding sequence of clone AS32\_1i deposited under accession number ATCC 98026; or the nucleotide sequence of a mature protein coding sequence of clone AS32\_1i deposited under accession number ATCC 98026. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AS32\_1i deposited under accession number ATCC 98026. In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequencé of SEQ ID NO:19 from amino acid 78 to amino acid 97. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:19 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:19, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:19 having biological activity, the fragment comprising the amino acid sequence from amino acid 102 to amino acid 111 of SEQ ID NO:19.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

20

10

15

- (a) the amino acid sequence of SEQ ID NO:19;
- (b) the amino acid sequence of SEQ ID NO:19 from amino acid 78 to amino acid 97;
- fragments of the amino acid sequence of SEQ ID NO:19, (c) each fragment comprising eight consecutive amino acids of SEQ ID NO:19; and

25

(d) the amino acid sequence encoded by the cDNA insert of clone AS32\_1i deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:19 or the amino acid sequence of SEQ ID NO:19 from amino acid 78 to amino acid 97. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:19 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:19, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:19, the fragment comprising the amino acid sequence from amino acid 102 to amino acid 111 of SEQ ID NO:19.

10

20

25

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

- 5 (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:21;
  - (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:21 from nucleotide 65 to nucleotide 490;
  - (c) a polynucleotide comprising the nucleotide sequence of SEQID NO:21 from nucleotide 137 to nucleotide 490;
    - (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AS34\_1i deposited under accession number ATCC 98026;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AS34\_1i deposited under accession number ATCC 98026;
  - (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AS34\_1i deposited under accession number ATCC 98026;
  - (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AS34\_1i deposited under accession number ATCC 98026;
  - (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:22;
  - (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:22 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:22;
  - (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and
- (k) a polynucleotide which encodes a species homologue of theprotein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:21 from nucleotide 65 to nucleotide 490; the nucleotide sequence of SEQ ID NO:21 from nucleotide 137 to nucleotide 490; the nucleotide sequence of the full-length protein coding sequence of clone AS34\_1i deposited under accession number ATCC 98026; or the

5

10

15

20

25

30

ID NO:23:

nucleotide sequence of a mature protein coding sequence of clone AS34\_1i deposited under accession number ATCC 98026. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AS34\_1i deposited under accession number ATCC 98026.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:22;
- (b) fragments of the amino acid sequence of SEQ ID NO:22, each fragment comprising eight consecutive amino acids of SEQ ID NO:22; and
- (c) the amino acid sequence encoded by the cDNA insert of clone AS34\_1i deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:22. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:22 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:22, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:22, the fragment comprising the amino acid sequence from amino acid 66 to amino acid 75 of SEQ ID NO:22.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:23 from nucleotide 225 to nucleotide 677;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:23 from nucleotide 387 to nucleotide 677;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AT205\_1i deposited under accession number ATCC 98026;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AT205\_1i deposited under accession number ATCC

98026;

10

- a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AT205\_1i deposited under accession number ATCC 98026;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AT205\_1i deposited under accession number ATCC 98026;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:24;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:24 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:24;
  - (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:23 from nucleotide 225 to nucleotide 677; the nucleotide sequence of SEQ ID NO:23 from nucleotide 387 to nucleotide 677; the nucleotide sequence of the full-length protein coding sequence of clone AT205\_1i deposited under accession number ATCC 98026; or the nucleotide sequence of a mature protein coding sequence of clone AT205\_1i deposited under accession number ATCC 98026. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AT205\_1i deposited under accession number ATCC 98026. In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:24 from amino acid 6 to amino acid 25. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:24 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:24, or a polynucleotide encoding a protein 30 comprising a fragment of the amino acid sequence of SEQ ID NO:24 having biological activity, the fragment comprising the amino acid sequence from amino acid 70 to amino acid 79 of SEQ ID NO:24.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected

from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:24;

(b) the amino acid sequence of SEQ ID NO:24 from amino acid 6 to amino acid 25;

5

- (c) fragments of the amino acid sequence of SEQ ID NO:24, each fragment comprising eight consecutive amino acids of SEQ ID NO:24; and
- (d) the amino acid sequence encoded by the cDNA insert of clone AT205\_1i deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:24 or the amino acid sequence of SEQ ID NO:24 from amino acid 6 to amino acid 25. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:24 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:24, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:24, the fragment comprising the amino acid sequence from amino acid 70 to amino acid 79 of SEQ ID NO:24.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:25;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ
   ID NO:25 from nucleotide 38 to nucleotide 832;

25

- a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AT211\_1i deposited under accession number ATCC 98026;
- (d) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AT211\_1i deposited under accession number ATCC 98026:
- (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AT211\_1i deposited under accession number ATCC 98026;
  - (f) a polynucleotide encoding a mature protein encoded by the

5

15

20

25

30

cDNA insert of clone AT211\_1i deposited under accession number ATCC 98026;

- (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:26;
- (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:26 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:26;
- (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and
- (j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:25 from nucleotide 38 to nucleotide 832; the nucleotide sequence of the full-length protein coding sequence of clone AT211\_1i deposited under accession number ATCC 98026; or the nucleotide sequence of a mature protein coding sequence of clone AT211\_1i deposited under accession number ATCC 98026. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AT211\_1i deposited under accession number ATCC 98026.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:26;
- (b) fragments of the amino acid sequence of SEQ ID NO:26, each fragment comprising eight consecutive amino acids of SEQ ID NO:26; and

the amino acid sequence encoded by the cDNA insert of

clone AT211\_1i deposited under accession number ATCC 98026; the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:26. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:26 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:26, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:26, the fragment comprising the amino acid sequence from amino acid 127 to amino acid 136 of SEQ ID NO:26.

(c)

In one embodiment, the present invention provides a composition

comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ
 ID NO:27;

5

- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:27 from nucleotide 194 to nucleotide 423;
- (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AT319\_1i deposited under accession number ATCC 98026;

10

15

- (d) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AT319\_1i deposited under accession number ATCC 98026;
- (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AT319\_1i deposited under accession number ATCC 98026;
- (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AT319\_1i deposited under accession number ATCC 98026;
- (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:28;

20

- (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:28 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:28;
- (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and

25

(j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:27 from nucleotide 194 to nucleotide 423; the nucleotide sequence of the full-length protein coding sequence of clone AT319\_1i deposited under accession number ATCC 98026; or the nucleotide sequence of a mature protein coding sequence of clone AT319\_1i deposited under accession number ATCC 98026. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AT319\_1i deposited under accession number ATCC 98026. In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence

of SEQ ID NO:28 from amino acid 2 to amino acid 21. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:28 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:28, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:28 having biological activity, the fragment comprising the amino acid sequence from amino acid 30 to amino acid 39 of SEQ ID NO:28.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

15

30

- (a) the amino acid sequence of SEQ ID NO:28;
- (b) the amino acid sequence of SEQ ID NO:28 from amino acid 2 to amino acid 21;
- (c) fragments of the amino acid sequence of SEQ ID NO:28, each fragment comprising eight consecutive amino acids of SEQ ID NO:28; and
  - (d) the amino acid sequence encoded by the cDNA insert of clone AT319\_1i deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:28 or the amino acid sequence of SEQ ID NO:28 from amino acid 2 to amino acid 21. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:28 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:28, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:28, the fragment comprising the amino acid sequence from amino acid 30 to amino acid 39 of SEQ ID NO:28.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:30;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:30 from nucleotide 61 to nucleotide 514;

5

10

15

20

- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:30 from nucleotide 112 to nucleotide 514;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AW191\_1i deposited under accession number ATCC 98026;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AW191\_1i deposited under accession number ATCC 98026;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AW191\_1i deposited under accession number ATCC 98026;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AW191\_1i deposited under accession number ATCC 98026;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:31;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:31 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:31;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:30 from nucleotide 61 to nucleotide 514; the nucleotide sequence of SEQ ID NO:30 from nucleotide 112 to nucleotide 514; the nucleotide sequence of the full-length protein coding sequence of clone AW191\_1i deposited under accession number ATCC 98026; or the nucleotide sequence of a mature protein coding sequence of clone AW191\_1i deposited under accession number ATCC 98026. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AW191\_1i deposited under accession number ATCC 98026. In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:31 from amino acid 24 to amino acid 43. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:31 having biological activity, the

5

25

30

fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:31, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:31 having biological activity, the fragment comprising the amino acid sequence from amino acid 70 to amino acid 79 of SEQ ID NO:31.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:31;
- 10 (b) the amino acid sequence of SEQ ID NO:31 from amino acid 24 to amino acid 43;
  - (c) fragments of the amino acid sequence of SEQ ID NO:31, each fragment comprising eight consecutive amino acids of SEQ ID NO:31; and
- (d) the amino acid sequence encoded by the cDNA insert of clone AW191\_1i deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:31 or the amino acid sequence of SEQ ID NO:31 from amino acid 24 to amino acid 43. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:31 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:31, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:31, the fragment comprising the amino acid sequence from amino acid 70 to amino acid 79 of SEO ID NO:31.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:33;
- (b) a polynucleotide comprising the nucleotide sequence of SEQID NO:33 from nucleotide 14 to nucleotide 391;
  - (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone BB9\_1i deposited under accession number ATCC 98026;

5

10

15

20

25

30

(d) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone BB9\_1i deposited under accession number ATCC 98026;

- (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone BB9\_1i deposited under accession number ATCC 98026:
- (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone BB9\_1i deposited under accession number ATCC 98026;
- (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:34;
  - (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:34 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:34;
  - (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and
  - (j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:33 from nucleotide 14 to nucleotide 391; the nucleotide sequence of the full-length protein coding sequence of clone BB9\_1i deposited under accession number ATCC 98026; or the nucleotide sequence of a mature protein coding sequence of clone BB9\_1i deposited under accession number ATCC 98026. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone BB9\_1i deposited under accession number ATCC 98026. In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:34 from amino acid 75 to amino acid 94. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:34 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:34, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:34 having biological activity, the fragment comprising the amino acid sequence from amino acid 55 to amino acid 64 of SEQ ID NO:34.

In other embodiments, the present invention provides a composition

comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:34;
- (b) the amino acid sequence of SEQ ID NO:34 from amino acid 75 to amino acid 94;
  - (c) fragments of the amino acid sequence of SEQ ID NO:34, each fragment comprising eight consecutive amino acids of SEQ ID NO:34; and
  - (d) the amino acid sequence encoded by the cDNA insert of clone BB9\_1i deposited under accession number ATCC 98026;
- the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:34 or the amino acid sequence of SEQ ID NO:34 from amino acid 75 to amino acid 94. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:34 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:34, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:34, the fragment comprising the amino acid sequence from amino acid 55 to amino acid 64 of SEQ ID NO:34.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:36;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:36 from nucleotide 58 to nucleotide 655;

25

- (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone H617\_1i deposited under accession number ATCC 98026;
- (d) a polynucleotide encoding the full-length protein encoded
   by the cDNA insert of clone H617\_1i deposited under accession number ATCC
   98026;
- (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone H617\_1i deposited under accession number ATCC 98026;

5

(f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone H617\_1i deposited under accession number ATCC 98026;

- $\mbox{(g)} \qquad \mbox{a polynucleotide encoding a protein comprising the amino} \\ \mbox{acid sequence of SEQ ID NO:37;}$
- (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:37 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:37;
- (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and
- 10 (j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:36 from nucleotide 58 to nucleotide 655; the nucleotide sequence of the full-length protein coding sequence of clone H617\_1i deposited under accession number ATCC 98026; or the nucleotide sequence of a mature protein coding sequence of clone H617\_1i deposited under accession number ATCC 98026. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone H617\_1i deposited under accession number ATCC 98026. In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:37 from amino acid 65 to amino acid 84. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:37 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:37, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:37 having biological activity, the fragment comprising the amino acid sequence from amino acid 95 to amino acid 104 of SEO ID NO:37.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:37;
- (b) the amino acid sequence of SEQ ID NO:37 from amino acid 65 to amino acid 84;
  - (c) fragments of the amino acid sequence of SEQ ID NO:37,

each fragment comprising eight consecutive amino acids of SEQ ID NO:37; and

(d) the amino acid sequence encoded by the cDNA insert of clone H617\_1i deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:37 or the amino acid sequence of SEQ ID NO:37 from amino acid 65 to amino acid 84: In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:37 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:37, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:37, the fragment comprising the amino acid sequence from amino acid 95 to amino acid 104 of SEQ ID NO:37.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

15

20

25

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:39;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:39 from nucleotide 71 to nucleotide 377;
- (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone K39\_1i deposited under accession number ATCC 98026;
- (d) a polynucleotide encoding the full-length protein encoded
   by the cDNA insert of clone K39\_1i deposited under accession number ATCC
   98026;
- (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone K39\_1i deposited under accession number ATCC 98026;
- (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone K39\_1i deposited under accession number ATCC 98026;
- (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:40;
- (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:40 having biological activity, the

fragment comprising eight consecutive amino acids of SEQ ID NO:40;

- (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and
- (j) a polynucleotide which encodes a species homologue of the5 protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:39 from nucleotide 71 to nucleotide 377; the nucleotide sequence of the full-length protein coding sequence of clone K39\_1i deposited under accession number ATCC 98026; or the nucleotide sequence of a mature protein coding sequence of clone K39\_1i deposited under accession number ATCC 98026. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone K39\_1i deposited under accession number ATCC 98026. In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:40 from amino acid 62 to amino acid 81.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

15

20

- (a) the amino acid sequence of SEQ ID NO:40;
- (b) the amino acid sequence of SEQ ID NO:40 from amino acid 62 to amino acid 81;
- (c) fragments of the amino acid sequence of SEQ ID NO:40, each fragment comprising eight consecutive amino acids of SEQ ID NO:40; and
- (d) the amino acid sequence encoded by the cDNA insert of clone K39\_1i deposited under accession number ATCC 98026;
- the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:40. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:40 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:40, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:40, the fragment comprising the amino acid sequence from amino acid 46 to amino acid 55 of SEQ ID NO:40.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group

5

10

15

20

25

consisting of:

- $\hbox{(a)} \qquad \hbox{a polynucleotide comprising the nucleotide sequence of SEQ} \\ \mbox{ID NO:42;}$
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:42 from nucleotide 1 to nucleotide 332;
  - (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone K640\_1i deposited under accession number ATCC 98026;
- (d) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone K640\_1i deposited under accession number ATCC 98026:
  - (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone K640\_1i deposited under accession number ATCC 98026;
- (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone K640\_1i deposited under accession number ATCC 98026;
  - (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:43;
- (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:43 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:43;
  - (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and
- (j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:42 from nucleotide 1 to nucleotide 332; the nucleotide sequence of the full-length protein coding sequence of clone K640\_1i deposited under accession number ATCC 98026; or the nucleotide sequence of a mature protein coding sequence of clone K640\_1i deposited under accession number ATCC 98026. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone K640\_1i deposited under accession number ATCC 98026. In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:43 from amino acid 11 to amino acid 30. In further preferred embodiments,

the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:43 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:43, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:43 having biological activity, the fragment comprising the amino acid sequence from amino acid 50 to amino acid 59 of SEQ ID NO:43.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

10

15

20

25

- (a) the amino acid sequence of SEQ ID NO:43;
- (b) the amino acid sequence of SEQ ID NO:43 from amino acid 11 to amino acid 30;
- (c) fragments of the amino acid sequence of SEQ ID NO:43, each fragment comprising eight consecutive amino acids of SEQ ID NO:43; and
- (d) the amino acid sequence encoded by the cDNA insert of clone K640\_1i deposited under accession number ATCC 98026;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:43 or the amino acid sequence of SEQ ID NO:43 from amino acid 11 to amino acid 30. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:43 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:43, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:43, the fragment comprising the amino acid sequence from amino acid 50 to amino acid 59 of SEQ ID NO:43.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQID NO:45;
  - (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:45 from nucleotide 12 to nucleotide 539;
    - (c) a polynucleotide comprising the nucleotide sequence of the

full-length protein coding sequence of clone AE402\_1i deposited under accession number ATCC 98190;

- (d) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AE402\_1i deposited under accession number ATCC 98190;
- (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AE402\_1i deposited under accession number ATCC 98190;
- (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AE402\_1i deposited under accession number ATCC 98190;

10

15

20

25

30

- (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:46;
- (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:46 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:46;
- (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and
- (j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:45 from nucleotide 12 to nucleotide 539; the nucleotide sequence of the full-length protein coding sequence of clone AE402\_1i deposited under accession number ATCC 98190; or the nucleotide sequence of a mature protein coding sequence of clone AE402\_1i deposited under accession number ATCC 98190. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AE402\_1i deposited under accession number ATCC 98190.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:46;
- (b) fragments of the amino acid sequence of SEQ ID NO:46, each fragment comprising eight consecutive amino acids of SEQ ID NO:46; and
- (c) the amino acid sequence encoded by the cDNA insert of clone AE402\_1i deposited under accession number ATCC 98190;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:46. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:46 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:46, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:46, the fragment comprising the amino acid sequence from amino acid 83 to amino acid 92 of SEQ ID NO:46.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:47;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:47 from nucleotide 61 to nucleotide 513;
  - (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:47 from nucleotide 322 to nucleotide 513;
  - (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AE610\_1i deposited under accession number ATCC 98190;

20

25

- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AE610\_1i deposited under accession number ATCC 98190;
- a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AE610\_1i deposited under accession number ATCC 98190;
  - (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AE610\_1i deposited under accession number ATCC 98190;
- (h) a polynucleotide encoding a protein comprising the amino
   acid sequence of SEQ ID NO:48;
  - (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:48 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:48;
    - (j) a polynucleotide which is an allelic variant of a

polynucleotide of (a)-(g) above; and

10

15

30

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:47 from nucleotide 61 to nucleotide 513; the nucleotide sequence of SEQ ID NO:47 from nucleotide 322 to nucleotide 513; the nucleotide sequence of the full-length protein coding sequence of clone AE610\_1i deposited under accession number ATCC 98190; or the nucleotide sequence of a mature protein coding sequence of clone AE610\_1i deposited under accession number ATCC 98190. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AE610\_1i deposited under accession number ATCC 98190.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:48;
- (b) fragments of the amino acid sequence of SEQ ID NO:48, each fragment comprising eight consecutive amino acids of SEQ ID NO:48; and
- (c) the amino acid sequence encoded by the cDNA insert of clone AE610\_1i deposited under accession number ATCC 98190;
- 20 the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:48. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:48 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:48, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:48, the fragment comprising the amino acid sequence from amino acid 70 to amino acid 79 of SEQ ID NO:48.

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:50;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:50 from nucleotide 20 to nucleotide 523;

5

10

15

20

- (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AH106\_1i deposited under accession number ATCC 98190;
- (d) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AH106\_1i deposited under accession number ATCC 98190:
- (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AH106\_1i deposited under accession number ATCC 98190;
- (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AH106\_1i deposited under accession number ATCC 98190;
  - (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:51;
  - (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:51 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:51;
    - (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and
- (j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:50 from nucleotide 20 to nucleotide 523; the nucleotide sequence of the full-length protein coding sequence of clone AH106\_1i deposited under accession number ATCC 98190; or the nucleotide sequence of a mature protein coding sequence of clone AH106\_1i deposited under accession number ATCC 98190. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AH106\_1i deposited under accession number ATCC 98190.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:51;
- (b) fragments of the amino acid sequence of SEQ ID NO:51, each fragment comprising eight consecutive amino acids of SEQ ID NO:51; and
  - (c) the amino acid sequence encoded by the cDNA insert of

clone AH106\_1i deposited under accession number ATCC 98190; the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:51. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:51 having biological activity, the fragment preferably

comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:51, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:51, the fragment comprising the amino acid sequence from amino acid 79 to amino acid 88 of SEQ ID NO:51.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

10

15

20

25

30

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:52;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:52 from nucleotide 130 to nucleotide 309;
- (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AH196\_1i deposited under accession number ATCC 98190;
- (d) a polynucleotide encoding the full-length protein encoded
   by the cDNA insert of clone AH196\_1i deposited under accession number ATCC
   98190;
- (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AH196\_1i deposited under accession number ATCC 98190;
- (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AH196\_1i deposited under accession number ATCC 98190;
- (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:53;
- (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:53 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:53;
- (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and

(j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:52 from nucleotide 130 to nucleotide 309; the nucleotide sequence of the full-length protein coding sequence of clone AH196\_1i deposited under accession number ATCC 98190; or the nucleotide sequence of a mature protein coding sequence of clone AH196\_1i deposited under accession number ATCC 98190. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AH196\_1i deposited under accession number ATCC 98190.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

10

15

25

30

- (a) the amino acid sequence of SEQ ID NO:53;
- (b) fragments of the amino acid sequence of SEQ ID NO:53, each fragment comprising eight consecutive amino acids of SEQ ID NO:53; and
- (c) the amino acid sequence encoded by the cDNA insert of clone AH196\_1i deposited under accession number ATCC 98190;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:53. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:53 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:53, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:53, the fragment comprising the amino acid sequence from amino acid 25 to amino acid 34 of SEQ ID NO:53.

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:55:
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:55 from nucleotide 69 to nucleotide 467;
- (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AI6\_1i deposited under accession

number ATCC 98190;

(d) a polynucleotide encoding the full-length protein encoded
 by the cDNA insert of clone AI6\_1i deposited under accession number ATCC
 98190;

5

- (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AI6\_1i deposited under accession number ATCC 98190;
- (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AI6\_1i deposited under accession number ATCC 98190;

10

- (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:56;
- (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:56 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:56;

15

20

- (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and
- (j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:55 from nucleotide 69 to nucleotide 467; the nucleotide sequence of the full-length protein coding sequence of clone AI6\_1i deposited under accession number ATCC 98190; or the nucleotide sequence of a mature protein coding sequence of clone AI6\_1i deposited under accession number ATCC 98190. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AI6\_1i deposited under accession number ATCC 98190. In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:56 from amino acid 69 to amino acid 133. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:56 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:56, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:56 having biological activity, the fragment comprising the amino acid sequence from amino acid 61 to amino acid 70 of SEQ ID NO:56.

5

25

30

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:56;
- (b) the amino acid sequence of SEQ ID NO:56 from amino acid 69 to amino acid 133;
- (c) fragments of the amino acid sequence of SEQ ID NO:56, each fragment comprising eight consecutive amino acids of SEQ ID NO:56; and
- (d) the amino acid sequence encoded by the cDNA insert of clone AI6\_1i deposited under accession number ATCC 98190;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:56 or the amino acid sequence of SEQ ID NO:56 from amino acid 69 to amino acid 133. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:56 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:56, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:56, the fragment comprising the amino acid sequence from amino acid 61 to amino acid 70 of SEQ ID NO:56.

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:58;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:58 from nucleotide 55 to nucleotide 363;
  - (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AJ13\_1i deposited under accession number ATCC 98190:
  - (d) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AJ13\_1i deposited under accession number ATCC 98190;
  - (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AJ13\_1i deposited under accession

number ATCC 98190;

5

10

15

25

- (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AJ13\_1i deposited under accession number ATCC 98190;
- (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:59;
  - (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:59 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:59;
- (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and
- (j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:58 from nucleotide 55 to nucleotide 363; the nucleotide sequence of the full-length protein coding sequence of clone AJ13\_1i deposited under accession number ATCC 98190; or the nucleotide sequence of a mature protein coding sequence of clone AJ13\_1i deposited under accession number ATCC 98190. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AJ13\_1i deposited under accession number ATCC 98190.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:59;
- (b) fragments of the amino acid sequence of SEQ ID NO:59, each fragment comprising eight consecutive amino acids of SEQ ID NO:59; and
- (c) the amino acid sequence encoded by the cDNA insert of clone AJ13\_1i deposited under accession number ATCC 98190;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:59. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:59 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:59, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:59, the fragment comprising the amino acid sequence from amino acid 46 to

amino acid 55 of SEQ ID NO:59.

5

10

15

20

25

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:60;
  - (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:60 from nucleotide 33 to nucleotide 422;
  - (c) a polynucleotide comprising the nucleotide sequence of SEQ
     ID NO:60 from nucleotide 114 to nucleotide 422;
    - (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AJ27\_1i deposited under accession number ATCC 98190;
    - (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AJ27\_1i deposited under accession number ATCC 98190;
    - (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AJ27\_1i deposited under accession number ATCC 98190:
    - (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AJ27\_1i deposited under accession number ATCC 98190;
    - (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:61;
    - (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:61 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:61;
    - (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and
- (k) a polynucleotide which encodes a species homologue of theprotein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:60 from nucleotide 33 to nucleotide 422; the nucleotide sequence of SEQ ID NO:60 from nucleotide 114 to nucleotide 422; the nucleotide sequence of the full-length protein coding sequence of clone AJ27\_1i deposited under accession number ATCC 98190; or the

nucleotide sequence of a mature protein coding sequence of clone AJ27\_1i deposited under accession number ATCC 98190. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AJ27\_1i deposited under accession number ATCC 98190.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

5

10

15

25

30

- (a) the amino acid sequence of SEQ ID NO:61;
- (b) fragments of the amino acid sequence of SEQ ID NO:61, each fragment comprising eight consecutive amino acids of SEQ ID NO:61; and
- (c) the amino acid sequence encoded by the cDNA insert of clone AJ27\_1i deposited under accession number ATCC 98190;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:61. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:61 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:61, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:61, the fragment comprising the amino acid sequence from amino acid 60 to amino acid 69 of SEQ ID NO:61.

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:63;
  - (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:63 from nucleotide 47 to nucleotide 517;
  - (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:63 from nucleotide 116 to nucleotide 517;
  - (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AJ142\_1i deposited under accession number ATCC 98190;
  - (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AJ142\_1i deposited under accession number ATCC

5

10

15

30

98190;

- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AJ142\_1i deposited under accession number ATCC 98190;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AJ142\_1i deposited under accession number ATCC 98190;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:64;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:64 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:64;
  - (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:63 from nucleotide 47 to nucleotide 517; the nucleotide sequence of SEQ ID NO:63 from nucleotide 116 to nucleotide 517; the nucleotide sequence of the full-length protein coding sequence of clone AJ142\_1i deposited under accession number ATCC 98190; or the nucleotide sequence of a mature protein coding sequence of clone AJ142\_1i deposited under accession number ATCC 98190. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AJ142\_1i deposited under accession number ATCC 98190.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:64;
- (b) fragments of the amino acid sequence of SEQ ID NO:64, each fragment comprising eight consecutive amino acids of SEQ ID NO:64; and
- (c) the amino acid sequence encoded by the cDNA insert of clone AJ142\_1i deposited under accession number ATCC 98190;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:64. In further preferred embodiments, the present invention provides a protein comprising a fragment of the

amino acid sequence of SEQ ID NO:64 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:64, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:64, the fragment comprising the amino acid sequence from amino acid 73 to amino acid 82 of SEQ ID NO:64.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ 10 ID NO:65;
  - (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:65 from nucleotide 312 to nucleotide 417;
  - (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AK604\_1i deposited under accession number ATCC 98190;
  - (d) a polynucleotide encoding the full-length protein encoded
     by the cDNA insert of clone AK604\_1i deposited under accession number ATCC
     98190;
- (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AK604\_1i deposited under accession number ATCC 98190;

15

25

30

- (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AK604\_1i deposited under accession number ATCC 98190;
- (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:66;
  - (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:66 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:66;
- (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and
  - (j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:65 from nucleotide 312 to nucleotide 417; the nucleotide sequence of the full-length

protein coding sequence of clone AK604\_1i deposited under accession number ATCC 98190; or the nucleotide sequence of a mature protein coding sequence of clone AK604\_1i deposited under accession number ATCC 98190. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AK604\_1i deposited under accession number ATCC 98190.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:66;
- (b) fragments of the amino acid sequence of SEQ ID NO:66, each fragment comprising eight consecutive amino acids of SEQ ID NO:66; and
  - (c) the amino acid sequence encoded by the cDNA insert of clone AK604\_1i deposited under accession number ATCC 98190;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:66. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:66 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:66, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:66, the fragment comprising the amino acid sequence from amino acid 12 to amino acid 21 of SEQ ID NO:66.

15

30

- 25 (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:68;
  - (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:68 from nucleotide 57 to nucleotide 353;
  - (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AK620\_1i deposited under accession number ATCC 98190;
    - (d) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AK620\_1i deposited under accession number ATCC 98190;

5

10

15

25

(e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AK620\_1i deposited under accession number ATCC 98190:

- (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AK620\_1i deposited under accession number ATCC 98190;
- (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:69;
- (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:69 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:69;
- (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and
- (j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:68 from nucleotide 57 to nucleotide 353; the nucleotide sequence of the full-length protein coding sequence of clone AK620\_1i deposited under accession number ATCC 98190; or the nucleotide sequence of a mature protein coding sequence of clone AK620\_1i deposited under accession number ATCC 98190. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AK620\_1i deposited under accession number ATCC 98190.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:69;
- (b) fragments of the amino acid sequence of SEQ ID NO:69, each fragment comprising eight consecutive amino acids of SEQ ID NO:69; and
- (c) the amino acid sequence encoded by the cDNA insert of clone AK620\_1i deposited under accession number ATCC 98190;
- the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:69. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:69 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino

acids of SEQ ID NO:69, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:69, the fragment comprising the amino acid sequence from amino acid 44 to amino acid 53 of SEQ ID NO:69.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

- $\hbox{(a)} \qquad \hbox{a polynucleotide comprising the nucleotide sequence of SEQ} \\ \hbox{ID NO:70;} \\$
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:70 from nucleotide 464 to nucleotide 751;

15

20

25

30

- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:70 from nucleotide 542 to nucleotide 751;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AK650\_1i deposited under accession number ATCC 98190;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AK650\_1i deposited under accession number ATCC 98190;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AK650\_1i deposited under accession number ATCC 98190;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AK650\_1i deposited under accession number ATCC 98190;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:71;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:71 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:71;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:70 from nucleotide 464 to nucleotide 751; the nucleotide sequence of SEQ ID NO:70

from nucleotide 542 to nucleotide 751; the nucleotide sequence of the full-length protein coding sequence of clone AK650\_1i deposited under accession number ATCC 98190; or the nucleotide sequence of a mature protein coding sequence of clone AK650\_1i deposited under accession number ATCC 98190. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AK650\_1i deposited under accession number ATCC 98190.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

10

25

30

- (a) the amino acid sequence of SEQ ID NO:71;
- (b) fragments of the amino acid sequence of SEQ ID NO:71, each fragment comprising eight consecutive amino acids of SEQ ID NO:71; and
- (c) the amino acid sequence encoded by the cDNA insert of clone AK650\_1i deposited under accession number ATCC 98190;
- the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:71. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:71 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:71, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:71, the fragment comprising the amino acid sequence from amino acid 43 to amino acid 52 of SEQ ID NO:71.

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:72;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:72 from nucleotide 116 to nucleotide 310;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:72 from nucleotide 173 to nucleotide 310;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AM226\_1i deposited under accession number ATCC 98190;

5

10

15

20

25

30

(e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AM226\_1i deposited under accession number ATCC 98190;

- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AM226\_1i deposited under accession number ATCC 98190;
  - (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AM226\_1i deposited under accession number ATCC 98190;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:73;
  - (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:73 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:73;
  - (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and
    - (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:72 from nucleotide 116 to nucleotide 310; the nucleotide sequence of SEQ ID NO:72 from nucleotide 173 to nucleotide 310; the nucleotide sequence of the full-length protein coding sequence of clone AM226\_1i deposited under accession number ATCC 98190; or the nucleotide sequence of a mature protein coding sequence of clone AM226\_1i deposited under accession number ATCC 98190. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AM226\_1i deposited under accession number ATCC 98190.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:73;
- (b) fragments of the amino acid sequence of SEQ ID NO:73, each fragment comprising eight consecutive amino acids of SEQ ID NO:73; and
- (c) the amino acid sequence encoded by the cDNA insert of clone AM226\_1i deposited under accession number ATCC 98190; the protein being substantially free from other mammalian proteins. Preferably such

protein comprises the amino acid sequence of SEQ ID NO:73. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:73 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:73, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:73, the fragment comprising the amino acid sequence from amino acid 27 to amino acid 36 of SEQ ID NO:73.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:75;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:75 from nucleotide 220 to nucleotide 453;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:75 from nucleotide 352 to nucleotide 453;

15

20

25

30

- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AR417\_1i deposited under accession number ATCC 98190;
- (e) a polynucleotide encoding the full-length protein encoded
   by the cDNA insert of clone AR417\_1i deposited under accession number ATCC
   98190;
  - a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AR417\_1i deposited under accession number ATCC 98190;
  - (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AR417\_1i deposited under accession number ATCC 98190;
  - (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:76;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:76 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:76;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:75 from nucleotide 220 to nucleotide 453; the nucleotide sequence of SEQ ID NO:75 from nucleotide 352 to nucleotide 453; the nucleotide sequence of the full-length protein coding sequence of clone AR417\_1i deposited under accession number ATCC 98190; or the nucleotide sequence of a mature protein coding sequence of clone AR417\_1i deposited under accession number ATCC 98190. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AR417\_1i deposited under accession number ATCC 98190.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:76;
- 15 (b) fragments of the amino acid sequence of SEQ ID NO:76, each fragment comprising eight consecutive amino acids of SEQ ID NO:76; and
  - (c) the amino acid sequence encoded by the cDNA insert of clone AR417\_1i deposited under accession number ATCC 98190;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:76. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:76 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:76, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:76, the fragment comprising the amino acid sequence from amino acid 34 to amino acid 43 of SEQ ID NO:76.

- 30 (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:77;
  - (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:77 from nucleotide 496 to nucleotide 583;
    - (c) a polynucleotide comprising the nucleotide sequence of SEQ

ID NO:77 from nucleotide 565 to nucleotide 583;

5

10

15

20

30

- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AU43\_1i deposited under accession number ATCC 98190;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AU43\_1i deposited under accession number ATCC 98190:
- a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AU43\_1i deposited under accession number ATCC 98190;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AU43\_1i deposited under accession number ATCC 98190;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:78;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:78 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:78;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:77 from nucleotide 496 to nucleotide 583; the nucleotide sequence of SEQ ID NO:77 from nucleotide 565 to nucleotide 583; the nucleotide sequence of the full-length protein coding sequence of clone AU43\_1i deposited under accession number ATCC 98190; or the nucleotide sequence of a mature protein coding sequence of clone AU43\_1i deposited under accession number ATCC 98190. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AU43\_1i deposited under accession number ATCC 98190.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:78;
- (b) fragments of the amino acid sequence of SEQ ID NO:78,

each fragment comprising eight consecutive amino acids of SEQ ID NO:78; and

(c) the amino acid sequence encoded by the cDNA insert of clone AU43\_1i deposited under accession number ATCC 98190;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:78. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:78 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:78, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:78, the fragment comprising the amino acid sequence from amino acid 9 to amino acid 18 of SEQ ID NO:78.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

15

20

25

30

- $\hbox{ (a) } \qquad \hbox{a polynucleotide comprising the nucleotide sequence of SEQ} \\ \hbox{ID NO:80;}$
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:80 from nucleotide 55 to nucleotide 405;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:80 from nucleotide 148 to nucleotide 405;
  - (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AW60\_1i deposited under accession number ATCC 98190;
  - (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AW60\_1i deposited under accession number ATCC 98190;
  - (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AW60\_1i deposited under accession number ATCC 98190;
  - (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AW60\_1i deposited under accession number ATCC 98190;
  - (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:81;
    - (i) a polynucleotide encoding a protein comprising a fragment

5

10

15

20

25

30

of the amino acid sequence of SEQ ID NO:81 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:81;

- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:80 from nucleotide 55 to nucleotide 405; the nucleotide sequence of SEQ ID NO:80 from nucleotide 148 to nucleotide 405; the nucleotide sequence of the full-length protein coding sequence of clone AW60\_1i deposited under accession number ATCC 98190; or the nucleotide sequence of a mature protein coding sequence of clone AW60\_1i deposited under accession number ATCC 98190. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AW60\_1i deposited under accession number ATCC 98190.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:81;
- (b) fragments of the amino acid sequence of SEQ ID NO:81, each fragment comprising eight consecutive amino acids of SEQ ID NO:81; and
- (c) the amino acid sequence encoded by the cDNA insert of clone AW60\_1i deposited under accession number ATCC 98190;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:81. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:81 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:81, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:81, the fragment comprising the amino acid sequence from amino acid 53 to amino acid 62 of SEQ ID NO:81.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ

ID NO:83;

5

10

15

20

- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:83 from nucleotide 256 to nucleotide 1338;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:83 from nucleotide 1120 to nucleotide 1338;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone BA176\_1i deposited under accession number ATCC 98190;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone BA176\_1i deposited under accession number ATCC 98190;
  - (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone BA176\_1i deposited under accession number ATCC 98190;
  - (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone BA176\_1i deposited under accession number ATCC 98190;
  - (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:84;
  - (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:84 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:84;
  - (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:83 from nucleotide 256 to nucleotide 1338; the nucleotide sequence of SEQ ID NO:83 from nucleotide 1120 to nucleotide 1338; the nucleotide sequence of the full-length protein coding sequence of clone BA176\_1i deposited under accession number ATCC 98190; or the nucleotide sequence of a mature protein coding sequence of clone BA176\_1i deposited under accession number ATCC 98190. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone BA176\_1i deposited under accession number ATCC 98190.

In other embodiments, the present invention provides a composition

comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:84;
- (b) fragments of the amino acid sequence of SEQ ID NO:84, each fragment comprising eight consecutive amino acids of SEQ ID NO:84; and
- (c) the amino acid sequence encoded by the cDNA insert of clone BA176\_1i deposited under accession number ATCC 98190;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:84. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:84 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:84, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:84, the fragment comprising the amino acid sequence from amino acid 175 to amino acid 184 of SEQ ID NO:84.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ
- 20 ID NO:85;

5

15

25

30

- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:85 from nucleotide 199 to nucleotide 396;
- (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone BD140\_1i deposited under accession number ATCC 98190;
- (d) a polynucleotide encoding the full-length protein encoded
   by the cDNA insert of clone BD140\_1i deposited under accession number ATCC
   98190;
- (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone BD140\_1i deposited under accession number ATCC 98190;
- a polynucleotide encoding a mature protein encoded by the cDNA insert of clone BD140\_1i deposited under accession number ATCC 98190;
  - (g) a polynucleotide encoding a protein comprising the amino

acid sequence of SEQ ID NO:86;

5

20

25

(h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:86 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:86;

- (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and
- (j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:85 from nucleotide 199 to nucleotide 396; the nucleotide sequence of the full-length protein coding sequence of clone BD140\_1i deposited under accession number ATCC 98190; or the nucleotide sequence of a mature protein coding sequence of clone BD140\_1i deposited under accession number ATCC 98190. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone BD140\_1i deposited under accession number ATCC 98190.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:86;
- (b) fragments of the amino acid sequence of SEQ ID NO:86, each fragment comprising eight consecutive amino acids of SEQ ID NO:86; and
  - (c) the amino acid sequence encoded by the cDNA insert of clone BD140\_1i deposited under accession number ATCC 98190;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:86. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:86 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:86, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:86, the fragment comprising the amino acid sequence from amino acid 28 to amino acid 37 of SEQ ID NO:86.

5

10

15

20

25

- PCT/US99/31005 a polynucleotide comprising the nucleotide sequence of SEQ (a) ID NO:87; a polynucleotide comprising the nucleotide sequence of (b) SEQ ID NO:87 from nucleotide 303 to nucleotide 617; a polynucleotide comprising the nucleotide sequence of SEQ (c) ID NO:87 from nucleotide 345 to nucleotide 617; (d)
  - a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone BD407\_1i deposited under accession number ATCC 98190;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone BD407\_1i deposited under accession number ATCC 98190;
  - (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone BD407\_1i deposited under accession number ATCC 98190;
  - a polynucleotide encoding a mature protein encoded by the (g) cDNA insert of clone BD407\_1i deposited under accession number ATCC 98190;
  - a polynucleotide encoding a protein comprising the amino (h) acid sequence of SEQ ID NO:88;
  - a polynucleotide encoding a protein comprising a fragment (i) of the amino acid sequence of SEQ ID NO:88 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:88;
  - a polynucleotide which is an allelic variant of a (j) polynucleotide of (a)-(g) above; and
  - a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:87 from nucleotide 303 to nucleotide 617; the nucleotide sequence of SEQ ID NO:87 from nucleotide 345 to nucleotide 617; the nucleotide sequence of the full-length protein coding sequence of clone BD407\_1i deposited under accession number ATCC 98190; or the nucleotide sequence of a mature protein coding sequence of clone BD407\_1i deposited under accession number ATCC 98190. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone BD407\_1i deposited under accession number ATCC 98190. In yet other preferred

embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:88 from amino acid 1 to amino acid 32. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:88 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:88, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:88 having biological activity, the fragment comprising the amino acid sequence from amino acid 47 to amino acid 56 of SEQ ID NO:88.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:88;
- (b) the amino acid sequence of SEQ ID NO:88 from amino acid 1 to amino acid 32;

15

- (c) fragments of the amino acid sequence of SEQ ID NO:88, each fragment comprising eight consecutive amino acids of SEQ ID NO:88; and
- (d) the amino acid sequence encoded by the cDNA insert of clone BD407\_1i deposited under accession number ATCC 98190;
- the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:88 or the amino acid sequence of SEQ ID NO:88 from amino acid 1 to amino acid 32. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:88 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:88, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:88, the fragment comprising the amino acid sequence from amino acid 47 to amino acid 56 of SEQ ID NO:88.

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:89:
  - (b) a polynucleotide comprising the nucleotide sequence of SEQ

5

10

15

20

ID NO:89 from nucleotide 152 to nucleotide 535;

- (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone BF290\_1i deposited under accession number ATCC 98190;
- (d) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone BF290\_1i deposited under accession number ATCC 98190;
- (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone BF290\_1i deposited under accession number ATCC 98190;
- a polynucleotide encoding a mature protein encoded by the cDNA insert of clone BF290\_1i deposited under accession number ATCC 98190;
- (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:90;
- (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:90 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:90;
- (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and
- (j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:89 from nucleotide 152 to nucleotide 535; the nucleotide sequence of the full-length protein coding sequence of clone BF290\_1i deposited under accession number ATCC 98190; or the nucleotide sequence of a mature protein coding sequence of clone BF290\_1i deposited under accession number ATCC 98190. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone BF290\_1i deposited under accession number ATCC 98190.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:90;
- (b) fragments of the amino acid sequence of SEQ ID NO:90, each fragment comprising eight consecutive amino acids of SEQ ID NO:90; and

(c) the amino acid sequence encoded by the cDNA insert of clone BF290\_1i deposited under accession number ATCC 98190;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:90. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:90 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:90, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:90, the fragment comprising the amino acid sequence from amino acid 59 to amino acid 68 of SEQ ID NO:90.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

15

20

25

30

ID NO:91;

- (a) a polynucleotide comprising the nucleotide sequence of SEQ
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:91 from nucleotide 160 to nucleotide 474;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:91 from nucleotide 331 to nucleotide 474;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone BG236\_1i deposited under accession number ATCC 98191;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone BG236\_1i deposited under accession number ATCC 98191;
- a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone BG236\_1i deposited under accession number ATCC 98191;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone BG236\_1i deposited under accession number ATCC 98191;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:92;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:92 having biological activity, the

5

20

30

fragment comprising eight consecutive amino acids of SEQ ID NO:92;

(j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and

(k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:91 from nucleotide 160 to nucleotide 474; the nucleotide sequence of SEQ ID NO:91 from nucleotide 331 to nucleotide 474; the nucleotide sequence of the full-length protein coding sequence of clone BG236\_1i deposited under accession number ATCC 98191; or the nucleotide sequence of a mature protein coding sequence of clone BG236\_1i deposited under accession number ATCC 98191. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone BG236\_1i deposited under accession number ATCC 98191.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:92;
- (b) fragments of the amino acid sequence of SEQ ID NO:92, each fragment comprising eight consecutive amino acids of SEQ ID NO:92; and
- (c) the amino acid sequence encoded by the cDNA insert of clone BG236\_1i deposited under accession number ATCC 98191;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:92. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:92 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:92, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:92, the fragment comprising the amino acid sequence from amino acid 47 to amino acid 56 of SEQ ID NO:92.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:93:

5

10

15

20

- (b) a polynucleotide comprising the nucleotide sequence of SEQID NO:93 from nucleotide 139 to nucleotide 419;
- (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone BG237\_1i deposited under accession number ATCC 98191;
- (d) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone BG237\_1i deposited under accession number ATCC 98191;
- (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone BG237\_1i deposited under accession number ATCC 98191;
- (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone BG237\_1i deposited under accession number ATCC 98191;
- (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:94;
  - (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:94 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:94;
  - (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and
  - (j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:93 from nucleotide 139 to nucleotide 419; the nucleotide sequence of the full-length protein coding sequence of clone BG237\_1i deposited under accession number ATCC 98191; or the nucleotide sequence of a mature protein coding sequence of clone BG237\_1i deposited under accession number ATCC 98191. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone BG237\_1i deposited under accession number ATCC 98191. In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:94 from amino acid 9 to amino acid 93. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:94 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty)

5

consecutive amino acids of SEQ ID NO:94, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:94 having biological activity, the fragment comprising the amino acid sequence from amino acid 41 to amino acid 50 of SEQ ID NO:94.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:94;
- (b) the amino acid sequence of SEQ ID NO:94 from amino acid 9 to amino acid 93;
  - (c) fragments of the amino acid sequence of SEQ ID NO:94, each fragment comprising eight consecutive amino acids of SEQ ID NO:94; and
  - (d) the amino acid sequence encoded by the cDNA insert of clone BG237\_1i deposited under accession number ATCC 98191;
- the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:94 or the amino acid sequence of SEQ ID NO:94 from amino acid 9 to amino acid 93. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:94 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:94, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:94, the fragment comprising the amino acid sequence from amino acid 41 to amino acid 50 of SEQ ID NO:94.

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:96;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ
   30 ID NO:96 from nucleotide 294 to nucleotide 431;
  - (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone BG255\_1i deposited under accession number ATCC 98191:
    - (d) a polynucleotide encoding the full-length protein encoded

5

by the cDNA insert of clone BG255\_1i deposited under accession number ATCC 98191;

- (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone BG255\_1i deposited under accession number ATCC 98191;
- (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone BG255\_1i deposited under accession number ATCC 98191;
- (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:97;
- 10 (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:97 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:97;
  - (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and
- 15 (j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:96 from nucleotide 294 to nucleotide 431; the nucleotide sequence of the full-length protein coding sequence of clone BG255\_1i deposited under accession number ATCC 98191; or the nucleotide sequence of a mature protein coding sequence of clone BG255\_1i deposited under accession number ATCC 98191. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone BG255\_1i deposited under accession number ATCC 98191.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:97;
- (b) fragments of the amino acid sequence of SEQ ID NO:97, each fragment comprising eight consecutive amino acids of SEQ ID NO:97; and
- 30 (c) the amino acid sequence encoded by the cDNA insert of clone BG255\_1i deposited under accession number ATCC 98191;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:97. In further preferred embodiments, the present invention provides a protein comprising a fragment of the

5

15

20

25

30

amino acid sequence of SEQ ID NO:97 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:97, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:97, the fragment comprising the amino acid sequence from amino acid 18 to amino acid 27 of SEQ ID NO:97.

- (a) a polynucleotide comprising the nucleotide sequence of SEQ 10 ID NO:99;
  - (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:99 from nucleotide 57 to nucleotide 968;
  - (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:99 from nucleotide 105 to nucleotide 968;
  - (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone H541\_3i deposited under accession number ATCC 98191;
  - (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone H541\_3i deposited under accession number ATCC 98191;
  - (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone H541\_3i deposited under accession number ATCC 98191;
  - (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone H541\_3i deposited under accession number ATCC 98191;
  - $\hbox{(h)} \qquad \hbox{a polynucleotide encoding a protein comprising the amino} \\$  acid sequence of SEQ ID NO:100;
  - (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:100 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:100;
  - (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and
  - (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:99 from nucleotide 57 to nucleotide 968; the nucleotide sequence of SEQ ID NO:99 from nucleotide 105 to nucleotide 968; the nucleotide sequence of the full-length protein coding sequence of clone H541\_3i deposited under accession number ATCC 98191; or the nucleotide sequence of a mature protein coding sequence of clone H541\_3i deposited under accession number ATCC 98191. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone H541\_3i deposited under accession number ATCC 98191.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:100;
- (b) fragments of the amino acid sequence of SEQ ID NO:100, each fragment comprising eight consecutive amino acids of SEQ ID NO:100; and
- 15 (c) the amino acid sequence encoded by the cDNA insert of clone H541\_3i deposited under accession number ATCC 98191;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:100. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:100 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:100, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:100, the fragment comprising the amino acid sequence from amino acid 147 to amino acid 156 of SEQ ID NO:100.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:101;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ
   ID NO:101 from nucleotide 37 to nucleotide 220;

30

(c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone H978\_1i deposited under accession number ATCC 98191;

5

10

15

20

(d) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone H978\_1i deposited under accession number ATCC 98191;

- (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone H978\_1i deposited under accession number ATCC 98191:
- (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone H978\_1i deposited under accession number ATCC 98191;
- (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:102;
  - (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:102 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:102;
- (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and
  - (j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:101 from nucleotide 37 to nucleotide 220; the nucleotide sequence of the full-length protein coding sequence of clone H978\_1i deposited under accession number ATCC 98191; or the nucleotide sequence of a mature protein coding sequence of clone H978\_1i deposited under accession number ATCC 98191. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone H978\_1i deposited under accession number ATCC 98191. In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:102 from amino acid 1 to amino acid 31. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:102 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:102, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:102 having biological activity, the fragment comprising the amino acid sequence from amino acid 25 to amino acid 34 of SEQ ID NO:102.

In other embodiments, the present invention provides a composition

5

25

30

comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:102;
- (b) the amino acid sequence of SEQ ID NO:102 from amino acid 1 to amino acid 31;
- (c) fragments of the amino acid sequence of SEQ ID NO:102, each fragment comprising eight consecutive amino acids of SEQ ID NO:102; and
- (d) the amino acid sequence encoded by the cDNA insert of clone H978\_1i deposited under accession number ATCC 98191;
- the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:102 or the amino acid sequence of SEQ ID NO:102 from amino acid 1 to amino acid 31. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:102 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:102, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:102, the fragment comprising the amino acid sequence from amino acid 25 to amino acid 34 of SEQ ID NO:102.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:104;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:104 from nucleotide 2 to nucleotide 422;
  - a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone L161\_1i deposited under accession number ATCC 98191;
- (d) a polynucleotide encoding the full-length protein encoded
   by the cDNA insert of clone L161\_1i deposited under accession number ATCC
   98191;
  - (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone L161\_1i deposited under accession number ATCC 98191;

5

10

 a polynucleotide encoding a mature protein encoded by the cDNA insert of clone L161\_1i deposited under accession number ATCC 98191;

- (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:105;
- (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:105 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:105;
- (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and
- (j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:104 from nucleotide 2 to nucleotide 422; the nucleotide sequence of the full-length protein coding sequence of clone L161\_1i deposited under accession number ATCC 98191; or the nucleotide sequence of a mature protein coding sequence of clone L161\_1i deposited under accession number ATCC 98191. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone L161\_1i deposited under accession number ATCC 98191. In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence 20 of SEQ ID NO:105 from amino acid 72 to amino acid 91. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:105 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:105, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:105 having biological activity, the fragment comprising the amino acid sequence from amino acid 65 to amino acid 74 of SEQ ID NO:105.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:105;
- (b) the amino acid sequence of SEQ ID NO:105 from amino acid 72 to amino acid 91;
  - (c) fragments of the amino acid sequence of SEQ ID NO:105,

each fragment comprising eight consecutive amino acids of SEQ ID NO:105; and

(d) the amino acid sequence encoded by the cDNA insert of clone L161\_1i deposited under accession number ATCC 98191;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:105 or the amino acid sequence of SEQ ID NO:105 from amino acid 72 to amino acid 91. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:105 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:105, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:105, the fragment comprising the amino acid sequence from amino acid 65 to amino acid 74 of SEQ ID NO:105.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

- $\hbox{ (a) } \qquad \hbox{a polynucleotide comprising the nucleotide sequence of SEQ} \\ \hbox{ID NO:107;}$
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:107 from nucleotide 73 to nucleotide 702;
- (c) a polynucleotide comprising the nucleotide sequence of SEQID NO:107 from nucleotide 118 to nucleotide 702;

20

25

- (d) a polynucleotide comprising the nucleotide sequence of the full- length protein coding sequence of clone AE648\_1i deposited under accession number ATCC 98237;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AE648\_1i deposited under accession number ATCC 98237;
  - a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AE648\_1i deposited under accession number ATCC 98237;
  - (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AE648\_1i deposited under accession number ATCC 98237;
  - (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:108;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:108 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:108;

- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:107 from nucleotide 73 to nucleotide 702; the nucleotide sequence of SEQ ID NO:107 from nucleotide 118 to nucleotide 702; the nucleotide sequence of the full-length protein coding sequence of clone AE648\_1i deposited under accession number ATCC 98237; or the nucleotide sequence of a mature protein coding sequence of clone AE648\_1i deposited under accession number ATCC 98237. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AE648\_1i deposited under accession number ATCC 98237. In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:108 from amino acid 1 to amino acid 34. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:108 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:108, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:108 having biological activity, the fragment comprising the amino acid sequence from amino acid 100 to amino acid 109 of SEQ ID NO:108.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:108;
- (b) the amino acid sequence of SEQ ID NO:108 from amino acid
- 30 1 to amino acid 34;

5

15

- (c) fragments of the amino acid sequence of SEQ ID NO:108,each fragment comprising eight consecutive amino acids of SEQ ID NO:108; and
- (d) the amino acid sequence encoded by the cDNA insert of clone AE648\_1i deposited under accession number ATCC 98237;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:108 or the amino acid sequence of SEQ ID NO:108 from amino acid 1 to amino acid 34. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:108 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:108, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:108, the fragment comprising the amino acid sequence from amino acid 100 to amino acid 109 of SEQ ID NO:108.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:109;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:109 from nucleotide 92 to nucleotide 268;
- (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AE693\_1i deposited under accession number ATCC 98237;
- (d) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AE693\_1i deposited under accession number ATCC 98237;
- (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AE693\_1i deposited under accession number ATCC 98237;
- (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AE693\_1i deposited under accession number ATCC 98237;
- $\mbox{(g)} \qquad \mbox{a polynucleotide encoding a protein comprising the amino} \\ \mbox{acid sequence of SEQ ID NO:110;} \\$
- (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:110 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:110;
- (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and

30

15

20

(j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:109 from nucleotide 92 to nucleotide 268; the nucleotide sequence of the full-length protein coding sequence of clone AE693\_1i deposited under accession number ATCC 98237; or the nucleotide sequence of a mature protein coding sequence of clone AE693\_1i deposited under accession number ATCC 98237. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AE693\_1i deposited under accession number ATCC 98237.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

15

20

25

- (a) the amino acid sequence of SEQ ID NO:110;
- $\mbox{(b)} \qquad \mbox{fragments of the amino acid sequence of SEQ ID NO:110,} \\ \mbox{each fragment comprising eight consecutive amino acids of SEQ ID NO:110;} \mbox{ and} \\ \mbox{}$
- (c) the amino acid sequence encoded by the cDNA insert of clone AE693\_1i deposited under accession number ATCC 98237;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:110. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:110 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:110, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:110, the fragment comprising the amino acid sequence from amino acid 24 to amino acid 33 of SEQ ID NO:110.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ 30 ID NO:112;
  - (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:112 from nucleotide 137 to nucleotide 412;
  - (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AK438\_1i deposited under accession

5

15

30

number ATCC 98237;

- (d) a polynucleotide encoding the full-length protein encoded
   by the cDNA insert of clone AK438\_1i deposited under accession number ATCC
   98237;
- (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AK438\_1i deposited under accession number ATCC 98237;
- (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AK438\_1i deposited under accession number ATCC 98237;
- 10 (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:113;
  - (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:113 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:113;
  - (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and
    - (j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:112 from nucleotide 137 to nucleotide 412; the nucleotide sequence of the full-length protein coding sequence of clone AK438\_1i deposited under accession number ATCC 98237; or the nucleotide sequence of a mature protein coding sequence of clone AK438\_1i deposited under accession number ATCC 98237. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AK438\_1i deposited under accession number ATCC 98237.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:113;
- (b) fragments of the amino acid sequence of SEQ ID NO:113, each fragment comprising eight consecutive amino acids of SEQ ID NO:113; and
- (c) the amino acid sequence encoded by the cDNA insert of clone AK438\_1i deposited under accession number ATCC 98237;

the protein being substantially free from other mammalian proteins. Preferably such

protein comprises the amino acid sequence of SEQ ID NO:113. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:113 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:113, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:113, the fragment comprising the amino acid sequence from amino acid 41 to amino acid 50 of SEQ ID NO:113.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

15

20

25

- $\hbox{(a)} \qquad \hbox{a polynucleotide comprising the nucleotide sequence of SEQ} \\$  ID NO:115;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:115 from nucleotide 1 to nucleotide 285;
- (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AK609\_1i deposited under accession number ATCC 98237;
- (d) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AK609\_1i deposited under accession number ATCC 98237;
- (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AK609\_1i deposited under accession number ATCC 98237;
- (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AK609\_1i deposited under accession number ATCC 98237;
- (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:116;
- (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:116 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:116;
- (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and
- (j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:115 from nucleotide 1 to nucleotide 285; the nucleotide sequence of the full-length protein coding sequence of clone AK609\_1i deposited under accession number ATCC 98237; or the nucleotide sequence of a mature protein coding sequence of clone AK609\_1i deposited under accession number ATCC 98237. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AK609\_1i deposited under accession number ATCC 98237.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:116;
- (b) fragments of the amino acid sequence of SEQ ID NO:116, each fragment comprising eight consecutive amino acids of SEQ ID NO:116; and
- (c) the amino acid sequence encoded by the cDNA insert of clone AK609\_1i deposited under accession number ATCC 98237; the protein being substantially free from other mammalian proteins. Preferably such

protein comprises the amino acid sequence of SEQ ID NO:116. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:116 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:116, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:116, the fragment comprising the amino acid sequence from amino acid 42 to amino acid 51 of SEQ ID NO:116.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:118;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:118 from nucleotide 43 to nucleotide 282;
  - (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:118 from nucleotide 118 to nucleotide 282;
  - (d) a polynucleotide comprising the nucleotide sequence of the full- length protein coding sequence of clone AM1060\_1i deposited under

5

10

15

30

accession number ATCC 98237;

- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AM1060\_1i deposited under accession number ATCC 98237:
- a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AM1060\_1i deposited under accession number ATCC 98237;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AM1060\_1i deposited under accession number ATCC 98237;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:119;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:119 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:119;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:118 from nucleotide 43 to nucleotide 282; the nucleotide sequence of SEQ ID NO:118 from nucleotide 118 to nucleotide 282; the nucleotide sequence of the full-length protein coding sequence of clone AM1060\_1i deposited under accession number ATCC 98237; or the nucleotide sequence of a mature protein coding sequence of clone AM1060\_1i deposited under accession number ATCC 98237. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AM1060\_1i deposited under accession number ATCC 98237.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:119;
- (b) fragments of the amino acid sequence of SEQ ID NO:119, each fragment comprising eight consecutive amino acids of SEQ ID NO:119; and
- (c) the amino acid sequence encoded by the cDNA insert of clone AM1060\_1i deposited under accession number ATCC 98237;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:119. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:119 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:119, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:119, the fragment comprising the amino acid sequence from amino acid 35 to amino acid 44 of SEQ ID NO:119.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:121;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:121 from nucleotide 316 to nucleotide 438;

20

25

- (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AQ2\_1i deposited under accession number ATCC 98237;
- (d) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AQ2\_1i deposited under accession number ATCC 98237;
- (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AQ2\_1i deposited under accession number ATCC 98237;
- (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AQ2\_1i deposited under accession number ATCC 98237;
- (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:122;
- (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:122 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:122;
- (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and
  - (j) a polynucleotide which encodes a species homologue of the

protein of (g) or (h) above.

25

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:121 from nucleotide 316 to nucleotide 438; the nucleotide sequence of the full-length protein coding sequence of clone AQ2\_1i deposited under accession number 5 ATCC 98237; or the nucleotide sequence of a mature protein coding sequence of clone AQ2\_1i deposited under accession number ATCC 98237. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AQ2\_1i deposited under accession number ATCC 98237. In yet other preferred embodiments, such polynucleotide encodes a protein comprising the 10 amino acid sequence of SEQ ID NO:122 from amino acid 1 to amino acid 25. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:122 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:122, or a polynucleotide 15 encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:122 having biological activity, the fragment comprising the amino acid sequence from amino acid 15 to amino acid 24 of SEQ ID NO:122.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:122;
- (b) the amino acid sequence of SEQ ID NO:122 from amino acid 1 to amino acid 25;
- (c) fragments of the amino acid sequence of SEQ ID NO:122, each fragment comprising eight consecutive amino acids of SEQ ID NO:122; and
- (d) the amino acid sequence encoded by the cDNA insert of clone AQ2\_1i deposited under accession number ATCC 98237;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:122 or the amino acid sequence of SEQ ID NO:122 from amino acid 1 to amino acid 25. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:122 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:122, or a protein comprising a fragment of the amino acid sequence of SEQ ID

NO:122, the fragment comprising the amino acid sequence from amino acid 15 to amino acid 24 of SEQ ID NO:122.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

5

15

20

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:124;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:124 from nucleotide 142 to nucleotide 285;
- 10 (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone K433\_1i deposited under accession number ATCC 98237;
  - (d) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone K433\_1i deposited under accession number ATCC 98237;
  - (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone K433\_1i deposited under accession number ATCC 98237:
  - (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone K433\_1i deposited under accession number ATCC 98237;
  - (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:125;
  - (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:125 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:125;
  - (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and
  - (j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.
- 30 Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:124 from nucleotide 142 to nucleotide 285; the nucleotide sequence of the full-length protein coding sequence of clone K433\_1i deposited under accession number ATCC 98237; or the nucleotide sequence of a mature protein coding sequence of clone K433\_1i deposited under accession number ATCC 98237. In other preferred

embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone K433\_1i deposited under accession number ATCC 98237. In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:125 from amino acid 1 to amino acid 30. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:125 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:125, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:125 having biological activity, the fragment comprising the amino acid sequence from amino acid 19 to amino acid 28 of SEQ ID NO:125.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

15 (a) the amino acid sequence of SEQ ID NO:125;

20

(b) the amino acid sequence of SEQ ID NO:125 from amino acid 1 to amino acid 30;

(c) fragments of the amino acid sequence of SEQ ID NO:125,each fragment comprising eight consecutive amino acids of SEQ ID NO:125; and

(d) the amino acid sequence encoded by the cDNA insert of clone K433\_1i deposited under accession number ATCC 98237;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:125 or the amino acid sequence of SEQ ID NO:125 from amino acid 1 to amino acid 30. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:125 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:125, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:125, the fragment comprising the amino acid sequence from amino acid 19 to amino acid 28 of SEO ID NO:125.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

(a) a polynucleotide comprising the nucleotide sequence of SEQ

ID NO:127:

5

15

20

- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:127 from nucleotide 47 to nucleotide 517;
- (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone L256\_1i deposited under accession number ATCC 98237;
- (d) a polynucleotide encoding the full-length protein encoded
   by the cDNA insert of clone L256\_1i deposited under accession number ATCC
   98237;
- 10 (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone L256\_1i deposited under accession number ATCC 98237;
  - (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone L256\_1i deposited under accession number ATCC 98237;
  - (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:128;
  - (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:128 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:128;
  - (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and
  - (j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

25 ID NO:127 from nucleotide 47 to nucleotide 517; the nucleotide sequence of the full-length protein coding sequence of clone L256\_1i deposited under accession number ATCC 98237; or the nucleotide sequence of a mature protein coding sequence of clone L256\_1i deposited under accession number ATCC 98237. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone L256\_1i deposited under accession number ATCC 98237. In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:128 from amino acid 8 to amino acid 157. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:128 having biological

activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:128, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:128 having biological activity, the fragment comprising the amino acid sequence from amino acid 73 to amino acid 82 of SEQ ID NO:128.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:128;
- 10 (b) the amino acid sequence of SEQ ID NO:128 from amino acid 8 to amino acid 157;
  - (c) fragments of the amino acid sequence of SEQ ID NO:128, each fragment comprising eight consecutive amino acids of SEQ ID NO:128; and
- (d) the amino acid sequence encoded by the cDNA insert of clone L256\_1i deposited under accession number ATCC 98237;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:128 or the amino acid sequence of SEQ ID NO:128 from amino acid 8 to amino acid 157. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:128 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:128, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:128, the fragment comprising the amino acid sequence from amino acid 73 to amino acid 82 of SEQ ID NO:128.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

25

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:130;
- (b) a polynucleotide comprising the nucleotide sequence of SEQID NO:130 from nucleotide 389 to nucleotide 694;
  - (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AM207\_1i deposited under accession number ATCC 98510;

5

10

15

25

30

- (d) a polynucleotide encoding the full-length protein encoded
   by the cDNA insert of clone AM207\_1i deposited under accession number ATCC
   98510;
- (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AM207\_1i deposited under accession number ATCC 98510;
  - (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AM207\_1i deposited under accession number ATCC 98510;
- (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:131;
  - (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:131 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:131;
  - (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and
  - (j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:130 from nucleotide 389 to nucleotide 694; the nucleotide sequence of the full-length protein coding sequence of clone AM207\_1i deposited under accession number ATCC 98510; or the nucleotide sequence of a mature protein coding sequence of clone AM207\_1i deposited under accession number ATCC 98510. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AM207\_1i deposited under accession number ATCC 98510.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:131;
- (b) fragments of the amino acid sequence of SEQ ID NO:131, each fragment comprising eight consecutive amino acids of SEQ ID NO:131; and
- (c) the amino acid sequence encoded by the cDNA insert of clone AM207\_1i deposited under accession number ATCC 98510;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:131. In further preferred

embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:131 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:131, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:131, the fragment comprising the amino acid sequence from amino acid 46 to amino acid 55 of SEQ ID NO:131.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

10

15

20

ID NO:133;

- (a) a polynucleotide comprising the nucleotide sequence of SEQ
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:133 from nucleotide 122 to nucleotide 685;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:133 from nucleotide 179 to nucleotide 685;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AM910\_1i deposited under accession number ATCC 98510;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AM910\_1i deposited under accession number ATCC 98510;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AM910\_1i deposited under accession number ATCC 98510;

25

- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AM910\_1i deposited under accession number ATCC 98510;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:134;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:134 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:134;
  - (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and
    - (k) a polynucleotide which encodes a species homologue of the

protein of (h) or (i) above.

25

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:133 from nucleotide 122 to nucleotide 685; the nucleotide sequence of SEQ ID NO:133 from nucleotide 179 to nucleotide 685; the nucleotide sequence of the full-length 5 protein coding sequence of clone AM910\_1i deposited under accession number ATCC 98510; or the nucleotide sequence of a mature protein coding sequence of clone AM910\_1i deposited under accession number ATCC 98510. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AM910\_1i deposited under accession number ATCC 98510. In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:134 from amino acid 85 to amino acid 139. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:134 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:134, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:134 having biological activity, the fragment comprising the amino acid sequence from amino acid 89 to amino acid 98 of SEQ ID NO:134.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:134;
- (b) the amino acid sequence of SEQ ID NO:134 from amino acid 85 to amino acid 139;
- (c) fragments of the amino acid sequence of SEQ ID NO:134, each fragment comprising eight consecutive amino acids of SEQ ID NO:134; and
- (d) the amino acid sequence encoded by the cDNA insert of clone AM910\_1i deposited under accession number ATCC 98510;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:134 or the amino acid sequence of SEQ ID NO:134 from amino acid 85 to amino acid 139. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:134 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino

acids of SEQ ID NO:134, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:134, the fragment comprising the amino acid sequence from amino acid 89 to amino acid 98 of SEQ ID NO:134.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:135;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:135 from nucleotide 84 to nucleotide 269;

15

20

25

30

- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:135 from nucleotide 144 to nucleotide 269;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AR54\_1i deposited under accession number ATCC 98510;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AR54\_1i deposited under accession number ATCC 98510;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AR54\_1i deposited under accession number ATCC 98510;
  - (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AR54\_1i deposited under accession number ATCC 98510;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:136;
  - (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:136 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:136;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and
  - (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:135 from nucleotide 84 to nucleotide 269; the nucleotide sequence of SEQ ID

NO:135 from nucleotide 144 to nucleotide 269; the nucleotide sequence of the full-length protein coding sequence of clone AR54\_1i deposited under accession number ATCC 98510; or the nucleotide sequence of a mature protein coding sequence of clone AR54\_1i deposited under accession number ATCC 98510. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AR54\_1i deposited under accession number ATCC 98510.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

10

25

30

- (a) the amino acid sequence of SEQ ID NO:136;
- (b) fragments of the amino acid sequence of SEQ ID NO:136, each fragment comprising eight consecutive amino acids of SEQ ID NO:136; and
- (c) the amino acid sequence encoded by the cDNA insert of clone AR54\_1i deposited under accession number ATCC 98510;
- the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:136. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:136 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:136, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:136, the fragment comprising the amino acid sequence from amino acid 26 to amino acid 35 of SEQ ID NO:136.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

- $\hbox{(a)} \qquad \hbox{a polynucleotide comprising the nucleotide sequence of SEQ} \\ \hbox{ID NO:137;}$
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:137 from nucleotide 32 to nucleotide 1300;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:137 from nucleotide 884 to nucleotide 1300;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone L200\_1i deposited under accession number ATCC 98510;

5

10

15

(e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone L200\_1i deposited under accession number ATCC 98510;

- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone L200\_1i deposited under accession number ATCC 98510;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone L200\_1i deposited under accession number ATCC 98510;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:138;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:138 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:138;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:137 from nucleotide 32 to nucleotide 1300; the nucleotide sequence of SEQ ID 20 NO:137 from nucleotide 884 to nucleotide 1300; the nucleotide sequence of the full-length protein coding sequence of clone L200\_1i deposited under accession number ATCC 98510; or the nucleotide sequence of a mature protein coding sequence of clone L200\_1i deposited under accession number ATCC 98510. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone L200\_1i deposited under accession number ATCC 98510. In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:138 from amino acid 1 to amino acid 144. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:138 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:138, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:138 having biological activity, the fragment comprising the amino acid sequence from amino acid 206 to amino acid 215 of SEQ ID NO:138.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:138;
- 5 (b) the amino acid sequence of SEQ ID NO:138 from amino acid 1 to amino acid 144;
  - (c) fragments of the amino acid sequence of SEQ ID NO:138, each fragment comprising eight consecutive amino acids of SEQ ID NO:138; and
- (d) the amino acid sequence encoded by the cDNA insert of clone L200\_1i deposited under accession number ATCC 98510;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:138 or the amino acid sequence of SEQ ID NO:138 from amino acid 1 to amino acid 144. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:138 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:138, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:138, the fragment comprising the amino acid sequence from amino acid 206 to amino acid 215 of SEQ ID NO:138.

15

25

30

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:139;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:139 from nucleotide 85 to nucleotide 1059;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:139 from nucleotide 151 to nucleotide 1059;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone WA129\_2i deposited under accession number ATCC 98510;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone WA129\_2i deposited under accession number ATCC 98510;

5

10

25

 a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone WA129\_2i deposited under accession number ATCC 98510;

- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone WA129\_2i deposited under accession number ATCC 98510;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:140;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:140 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:140;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

ID NO:139 from nucleotide 85 to nucleotide 1059; the nucleotide sequence of SEQ ID NO:139 from nucleotide 151 to nucleotide 1059; the nucleotide sequence of the full-length protein coding sequence of clone WA129\_2i deposited under accession number ATCC 98510; or the nucleotide sequence of a mature protein coding sequence of clone WA129\_2i deposited under accession number ATCC 98510. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone WA129\_2i deposited under accession number ATCC 98510.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:140;
- (b) fragments of the amino acid sequence of SEQ ID NO:140, each fragment comprising eight consecutive amino acids of SEQ ID NO:140; and
- (c) the amino acid sequence encoded by the cDNA insert of clone WA129\_2i deposited under accession number ATCC 98510; the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:140. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:140 having biological activity, the fragment preferably

comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:140, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:140, the fragment comprising the amino acid sequence from amino acid 157 to amino acid 166 of SEQ ID NO:140.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:141;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:141 from nucleotide 128 to nucleotide 643;
- (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:141 from nucleotide 197 to nucleotide 643;
- (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone WA154\_3i deposited under accession number ATCC 98510;
- (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone WA154\_3i deposited under accession number ATCC 98510;
- (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone WA154\_3i deposited under accession number ATCC 98510;
- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone WA154\_3i deposited under accession number ATCC 98510;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:142;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:142 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:142;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

95

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ

20

15

25

ID NO:141 from nucleotide 128 to nucleotide 643; the nucleotide sequence of SEQ ID NO:141 from nucleotide 197 to nucleotide 643; the nucleotide sequence of the full-length protein coding sequence of clone WA154\_3i deposited under accession number ATCC 98510; or the nucleotide sequence of a mature protein coding sequence of clone WA154\_3i deposited under accession number ATCC 98510. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone WA154\_3i deposited under accession number ATCC 98510. In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:142 from amino acid 37 to amino acid 77. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein 10 comprising a fragment of the amino acid sequence of SEQ ID NO:142 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:142, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:142 having biological activity, the fragment comprising the amino acid sequence from amino acid 81 to amino acid 90 of SEQ ID NO:142.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

20

- (a) the amino acid sequence of SEQ ID NO:142;
- $\mbox{(b)} \qquad \mbox{the amino acid sequence of SEQ ID NO:142 from amino acid} \label{eq:37}$  to amino acid 77;
- (c) fragments of the amino acid sequence of SEQ ID NO:142, each fragment comprising eight consecutive amino acids of SEQ ID NO:142; and
- 25 (d) the amino acid sequence encoded by the cDNA insert of clone WA154\_3i deposited under accession number ATCC 98510;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:142 or the amino acid sequence of SEQ ID NO:142 from amino acid 37 to amino acid 77. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:142 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:142, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:142, the fragment comprising the amino acid sequence from amino acid 81

to amino acid 90 of SEQ ID NO:142.

10

15

20

25

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:143;
  - (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:143 from nucleotide 51 to nucleotide 815;
  - (c) a polynucleotide comprising the nucleotide sequence of SEQID NO:143 from nucleotide 96 to nucleotide 815;
    - (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AA36\_1i deposited under accession number ATCC XXXXX;
  - (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AA36\_1i deposited under accession number ATCC XXXXX;
    - (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AA36\_1i deposited under accession number ATCC XXXXX;
    - (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AA36\_1i deposited under accession number ATCC XXXXX;
    - (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:144;
    - (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:144 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:144;
    - (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:143 from nucleotide 51 to nucleotide 815; the nucleotide sequence of SEQ ID NO:143 from nucleotide 96 to nucleotide 815; the nucleotide sequence of the full-length protein coding sequence of clone AA36\_1i deposited under accession number ATCC

XXXXX; or the nucleotide sequence of a mature protein coding sequence of clone AA36\_1i deposited under accession number ATCC XXXXX. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AA36\_1i deposited under accession number ATCC XXXXX. In yet other preferred embodiments, such polynucleotide encodes a protein comprising the amino acid sequence of SEQ ID NO:144 from amino acid 1 to amino acid 136. In further preferred embodiments, the present invention provides a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:144 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:144, or a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:144 having biological activity, the fragment comprising the amino acid sequence from amino acid 122 to amino acid 131 of SEQ ID NO:144.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

20

- (a) the amino acid sequence of SEQ ID NO:144;
- (b) the amino acid sequence of SEQ ID NO:144 from amino acid 1 to amino acid 136;
- (c) fragments of the amino acid sequence of SEQ ID NO:144, each fragment comprising eight consecutive amino acids of SEQ ID NO:144; and
- (d) the amino acid sequence encoded by the cDNA insert of clone AA36\_1i deposited under accession number ATCC XXXXX;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:144 or the amino acid sequence of SEQ ID NO:144 from amino acid 1 to amino acid 136. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:144 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:144, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:144, the fragment comprising the amino acid sequence from amino acid 122 to amino acid 131 of SEQ ID NO:144.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group

10

15

20

25

consisting of:

- $\hbox{(a)} \qquad \hbox{a polynucleotide comprising the nucleotide sequence of SEQ} \\ \mbox{ID NO:145;}$
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:145 from nucleotide 76 to nucleotide 594;
  - (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AC175\_2i deposited under accession number ATCC XXXXX;
- (d) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AC175\_2i deposited under accession number ATCC XXXXX;
  - (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AC175\_2i deposited under accession number ATCC XXXXX;
  - (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AC175\_2i deposited under accession number ATCC XXXXX;
    - (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:146;
  - (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:146 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:146;
    - (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and
- (j) a polynucleotide which encodes a species homologue of the protein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:145 from nucleotide 76 to nucleotide 594; the nucleotide sequence of the full-length protein coding sequence of clone AC175\_2i deposited under accession number ATCC XXXXX; or the nucleotide sequence of a mature protein coding sequence of clone AC175\_2i deposited under accession number ATCC XXXXX. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AC175\_2i deposited under accession number ATCC XXXXX.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected

from the group consisting of:

5

15

20

25

30

- (a) the amino acid sequence of SEQ ID NO:146;
- (b) fragments of the amino acid sequence of SEQ ID NO:146, each fragment comprising eight consecutive amino acids of SEQ ID NO:146; and
- (c) the amino acid sequence encoded by the cDNA insert of clone AC175\_2i deposited under accession number ATCC XXXXX;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:146. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:146 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:146, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:146, the fragment comprising the amino acid sequence from amino acid 81 to amino acid 90 of SEQ ID NO:146.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:147;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:147 from nucleotide 387 to nucleotide 734;
  - (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:147 from nucleotide 639 to nucleotide 734;
  - (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AV189\_1i deposited under accession number ATCC XXXXX;
  - (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AV189\_1i deposited under accession number ATCC XXXXX:
  - (f) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AV189\_1i deposited under accession number ATCC XXXXX;
  - (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AV189\_1i deposited under accession number ATCC XXXXX;

5

10

15

20

 (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:148;

- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:148 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:148;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and
- (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:147 from nucleotide 387 to nucleotide 734; the nucleotide sequence of SEQ ID NO:147 from nucleotide 639 to nucleotide 734; the nucleotide sequence of the full-length protein coding sequence of clone AV189\_1i deposited under accession number ATCC XXXXX; or the nucleotide sequence of a mature protein coding sequence of clone AV189\_1i deposited under accession number ATCC XXXXX. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone AV189\_1i deposited under accession number ATCC XXXXX.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:148;
- (b) fragments of the amino acid sequence of SEQ ID NO:148, each fragment comprising eight consecutive amino acids of SEQ ID NO:148; and
- (c) the amino acid sequence encoded by the cDNA insert of clone AV189\_1i deposited under accession number ATCC XXXXX;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:148. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:148 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:148, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:148, the fragment comprising the amino acid sequence from amino acid 53 to amino acid 62 of SEQ ID NO:148.

In one embodiment, the present invention provides a composition

5

10

15

20

25

comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:149;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:149 from nucleotide 66 to nucleotide 827;
  - (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:149 from nucleotide 366 to nucleotide 827;
  - (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone K368\_1i deposited under accession number ATCC XXXXX;
  - (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone K368\_1i deposited under accession number ATCC XXXXX;
- a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone K368\_1i deposited under accession number ATCC XXXXX;
  - (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone K368\_1i deposited under accession number ATCC XXXXX;
  - (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:150;
  - (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:150 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:150;
  - (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and
  - (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:149 from nucleotide 66 to nucleotide 827; the nucleotide sequence of SEQ ID NO:149 from nucleotide 366 to nucleotide 827; the nucleotide sequence of the full-length protein coding sequence of clone K368\_1i deposited under accession number ATCC XXXXX; or the nucleotide sequence of a mature protein coding sequence of clone K368\_1i deposited under accession number ATCC XXXXX. In other preferred embodiments, the

polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone K368\_1i deposited under accession number ATCC XXXXX.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:150;
- (b) fragments of the amino acid sequence of SEQ ID NO:150, each fragment comprising eight consecutive amino acids of SEQ ID NO:150; and

the amino acid sequence encoded by the cDNA insert of

10 clone K368\_1i deposited under accession number ATCC XXXXX;
the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:150. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:150 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino

to amino acid 131 of SEQ ID NO:150.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group

consisting of:

25

30

acids of SEQ ID NO:150, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:150, the fragment comprising the amino acid sequence from amino acid 122

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:151:
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:151 from nucleotide 219 to nucleotide 668;
  - (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:151 from nucleotide 426 to nucleotide 668;
  - (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone K568\_1i deposited under accession number ATCC XXXXX;
  - (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone K568\_1i deposited under accession number ATCC XXXXX;
    - (f) a polynucleotide comprising the nucleotide sequence of a

5

10

25

mature protein coding sequence of clone K568\_1i deposited under accession number ATCC XXXXX;

- (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone K568\_1i deposited under accession number ATCC XXXXX;
- (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:152;
- (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:152 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:152;
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above; and
  - (k) a polynucleotide which encodes a species homologue of the protein of (h) or (i) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:151 from nucleotide 219 to nucleotide 668; the nucleotide sequence of SEQ ID NO:151 from nucleotide 426 to nucleotide 668; the nucleotide sequence of the full-length protein coding sequence of clone K568\_1i deposited under accession number ATCC XXXXX; or the nucleotide sequence of a mature protein coding sequence of clone K568\_1i deposited under accession number ATCC XXXXX. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone K568\_1i deposited under accession number ATCC XXXXX.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:152;
- (b) fragments of the amino acid sequence of SEQ ID NO:152, each fragment comprising eight consecutive amino acids of SEQ ID NO:152; and
- (c) the amino acid sequence encoded by the cDNA insert of clone K568\_1i deposited under accession number ATCC XXXXX;
- the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:152. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:152 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino

acids of SEQ ID NO:152, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:152, the fragment comprising the amino acid sequence from amino acid 70 to amino acid 79 of SEQ ID NO:152.

In one embodiment, the present invention provides a composition comprising an isolated protein encoded by a polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:153;
- (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:153 from nucleotide 14 to nucleotide 1438;
  - (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone T85\_1i deposited under accession number ATCC XXXXX;
  - (d) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone T85\_1i deposited under accession number ATCC XXXXX;

15

20

25

- (e) a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone T85\_1i deposited under accession number ATCC XXXXX;
- (f) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone T85\_1i deposited under accession number ATCC XXXXX;
- (g) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:154;
- (h) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:154 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:154;
- (i) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above; and
- (j) a polynucleotide which encodes a species homologue of theprotein of (g) or (h) above.

Preferably, such polynucleotide comprises the nucleotide sequence of SEQ ID NO:153 from nucleotide 14 to nucleotide 1438; the nucleotide sequence of the full-length protein coding sequence of clone T85\_1i deposited under accession number ATCC XXXXX; or the nucleotide sequence of a mature protein coding sequence of clone

T85\_1i deposited under accession number ATCC XXXXX. In other preferred embodiments, the polynucleotide encodes the full-length or a mature protein encoded by the cDNA insert of clone T85\_1i deposited under accession number ATCC XXXXX.

In other embodiments, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:154;
- (b) fragments of the amino acid sequence of SEQ ID NO:154, each fragment comprising eight consecutive amino acids of SEQ ID NO:154; and
- 10 (c) the amino acid sequence encoded by the cDNA insert of clone T85\_1i deposited under accession number ATCC XXXXX;

the protein being substantially free from other mammalian proteins. Preferably such protein comprises the amino acid sequence of SEQ ID NO:154. In further preferred embodiments, the present invention provides a protein comprising a fragment of the amino acid sequence of SEQ ID NO:154 having biological activity, the fragment preferably comprising eight (more preferably twenty, most preferably thirty) consecutive amino acids of SEQ ID NO:154, or a protein comprising a fragment of the amino acid sequence of SEQ ID NO:154, the fragment comprising the amino acid sequence from amino acid 232 to amino acid 241 of SEQ ID NO:154.

Protein compositions of the present invention may further comprise a pharmaceutically acceptable carrier. Compositions comprising an antibody which specifically reacts with such protein are also provided by the present invention.

Methods are also provided for preventing, treating or ameliorating a medical condition which comprises administering to a mammalian subject a therapeutically effective amount of a composition comprising a protein of the present invention and a pharmaceutically acceptable carrier.

## BRIEF DESCRIPTION OF THE DRAWINGS

Figures 1A and 1B are schematic representations of the pED6 and pNOTs vectors, respectively, used for deposit of clones disclosed herein.

## **DETAILED DESCRIPTION**

## **ISOLATED PROTEINS**

20

30

Nucleotide and amino acid sequences, as presently determined, are

PCT/US99/31005 WO 00/37630

reported below for each clone and protein disclosed in the present application. The nucleotide sequence of each clone can readily be determined by sequencing of the deposited clone in accordance with known methods. The predicted amino acid sequence (both full-length and mature forms) can then be determined from such nucleotide 5 sequence. The amino acid sequence of the protein encoded by a particular clone can also be determined by expression of the clone in a suitable host cell, collecting the protein and determining its sequence. For each disclosed protein applicants have identified what they have determined to be the reading frame best identifiable with sequence information available at the time of filing.

As used herein a "secreted" protein is one which, when expressed in a suitable host cell, is transported across or through a membrane, including transport as a result of signal sequences in its amino acid sequence. "Secreted" proteins include without limitation proteins secreted wholly (e.g., soluble proteins) or partially (e.g., receptors) from the cell in which they are expressed. "Secreted" proteins also include without 15 limitation proteins which are transported across the membrane of the endoplasmic reticulum.

#### Protein "AK296\_1i"

10

30

One protein of the present invention has been identified as protein 20 "AK296\_1i". A partial cDNA clone encoding AK296\_1i was first isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AK296\_1i".

Applicants' methods identified clone AK296\_1i as encoding a secreted protein.

The nucleotide sequence of AK296\_1i as presently determined is reported in SEQ ID NO:1, and includes the poly(A) tail. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AK296\_1i protein

corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:2.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AK296\_1i should be approximately 1264 bp.

AK296\_1i protein was expressed in a Baculovirus expression system, and an expressed protein band of approximately 20 kDa detected in a membrane fraction using SDS polyacrylamide gel electrophoresis.

# Protein "AK533 1i"

20

25

One protein of the present invention has been identified as protein "AK533\_1i". A partial cDNA clone encoding AK533\_1i was first isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AK533\_1i".

Applicants' methods identified clone AK533\_1i as encoding a secreted protein.

The nucleotide sequence of AK533\_1i as presently determined is reported in SEQ ID NO:3, and includes the poly(A) tail. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AK533\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:4.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AK533\_1i should be approximately 1751 bp.

AK533\_1i protein was expressed in a COS cell expression system, and an expressed protein band of approximately 47 kDa detected in conditioned medium and membrane fractions using SDS polyacrylamide gel electrophoresis.

# Protein "AK583\_1i"

One protein of the present invention has been identified as protein "AK583\_1i". A partial cDNA clone encoding AK583\_1i was first isolated from a human

fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AK583\_1i".

Applicants' methods identified clone AK583\_1i as encoding a secreted protein.

The nucleotide sequence of AK583\_1i as presently determined is reported in SEQ ID NO:5, and includes the poly(A) tail. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AK583\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:6. Amino acids 12 to 24 of SEQ ID NO:6 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 25. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the AK583\_1i protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AK583\_1i should be approximately 870 bp.

## Protein "AM282\_1i"

10

15

20

One protein of the present invention has been identified as protein "AM282\_1i". A partial cDNA clone encoding AM282\_1i was first isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR,

including a poly(A) tail. This full-length clone is also referred to herein as "AM282\_1i".

Applicants' methods identified clone AM282\_1i as encoding a secreted protein.

The nucleotide sequence of AM282\_1i as presently determined is reported in SEQ ID NO:7, and includes the poly(A) tail. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AM282\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:8. Amino acids 12 to 24 of SEQ ID NO:8 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 25. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the AM282\_1i protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AM282\_1i should be approximately 1750 bp.

AM282\_1i protein was expressed in a Baculovirus expression system, and an expressed protein band of approximately 54 kDa detected in a conditioned medium fraction using SDS polyacrylamide gel electrophoresis.

# Protein "AM340\_1i"

15

One protein of the present invention has been identified as protein "AM340\_1i". A partial cDNA clone encoding AM340\_1i was first isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AM340\_1i".

Applicants' methods identified clone AM340\_1i as encoding a secreted protein.

The nucleotide sequence of AM340\_1i as presently determined is reported in SEQ ID NO:9, and includes the poly(A) tail. What applicants believe is the proper

reading frame and the predicted amino acid sequence of the AM340\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:10. Amino acids 85 to 97 of SEQ ID NO:10 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 98. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the AM340\_1i protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AM340\_1i should be approximately 650 bp.

AM340\_1i protein was expressed in a Baculovirus expression system, and an expressed protein band of approximately 27 kDa detected in a membrane fraction using SDS polyacrylamide gel electrophoresis.

# Protein "AM610 1i"

10

One protein of the present invention has been identified as protein "AM610\_1i". A partial cDNA clone encoding AM610\_1i was first isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AM610\_1i".

Applicants' methods identified clone AM610\_1i as encoding a secreted protein.

The nucleotide sequence of AM610\_1i as presently determined is reported in SEQ ID NO:11, and includes the poly(A) tail. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AM610\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:12. Amino acids 11 to 23 of SEQ ID NO:12 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 24. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain

should the predicted leader/signal sequence not be separated from the remainder of the AM610\_1i protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AM610\_1i should be approximately 1900 bp.

AM610\_1i protein was expressed in a COS cell expression system, and an expressed protein band of approximately 23 kDa detected in conditioned medium and membrane fractions using SDS polyacrylamide gel electrophoresis.

#### Protein "AP162\_1i"

5

One protein of the present invention has been identified as protein "AP162\_1i". A partial cDNA clone encoding AP162\_1i was first isolated from a human fetal placenta cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AP162\_1i".

Applicants' methods identified clone AP162\_1i as encoding a secreted protein.

The nucleotide sequence of the 5' portion of AP162\_1i as presently determined is reported in SEQ ID NO:13. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AP162\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:14. Additional nucleotide sequence from the 3' portion of AP162\_1i, including a poly(A) tail, is reported in SEQ ID NO:15.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AP162\_1i should be approximately 1200 bp.

AP162\_1i protein was expressed in a Baculovirus expression system, and an expressed protein band of approximately 20 kDa detected in a membrane fraction using SDS polyacrylamide gel electrophoresis.

# Protein "AR260 1i"

One protein of the present invention has been identified as protein "AR260\_1i". A partial cDNA clone encoding AR260\_1i was first isolated from a human adult retina cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AR260\_1i".

Applicants' methods identified clone AR260\_1i as encoding a secreted protein.

The nucleotide sequence of AR260\_1i as presently determined is reported in SEQ ID NO:16, and includes the poly(A) tail. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AR260\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:17.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AR260\_1i should be approximately 1900 bp.

AR260\_1i protein was expressed in a COS cell expression system, and an expressed protein band of approximately 27 kDa detected in conditioned medium and membrane fractions using SDS polyacrylamide gel electrophoresis.

# 25 Protein "AS32 1i"

15

One protein of the present invention has been identified as protein "AS32\_1i". A partial cDNA clone encoding AS32\_1i was first isolated from a human fetal brain cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor

was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AS32\_1i".

Applicants' methods identified clone AS32\_1i as encoding a secreted protein.

The nucleotide sequence of the 5' portion of AS32\_1i as presently determined is reported in SEQ ID NO:18. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AS32\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:19. Additional nucleotide sequence from the 3' portion of AS32\_1i, including a poly(A) tail, is reported in SEQ ID NO:20.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AS32\_1i should be approximately 1100 bp.

# Protein "AS34 1i"

5

10

One protein of the present invention has been identified as protein "AS34\_1i". A partial cDNA clone encoding AS34\_1i was first isolated from a human fetal brain cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AS34\_1i".

Applicants' methods identified clone AS34\_1i as encoding a secreted protein.

The nucleotide sequence of AS34\_1i as presently determined is reported in SEQ ID NO:21, and includes the poly(A) tail. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AS34\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:22. Amino acids 12 to 24 of SEQ ID NO:22 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 25. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain

should the predicted leader/signal sequence not be separated from the remainder of the AS34\_1i protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AS34\_1i should be approximately 550 bp.

AS34\_1i protein was expressed in a COS cell expression system, and an expressed protein band of approximately 8 kDa detected in conditioned medium and membrane fractions using SDS polyacrylamide gel electrophoresis.

# Protein "AT205 1i"

One protein of the present invention has been identified as protein "AT205\_1i". A partial cDNA clone encoding AT205\_1i was first isolated from a human adult blood (lymphocytes and dendritic cells, treated with mixed lymphocyte reaction) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR. This full-length clone is also referred to herein as "AT205\_1i".

Applicants' methods identified clone AT205\_1i as encoding a secreted protein.

The nucleotide sequence of AT205\_1i as presently determined is reported in SEQ ID NO:23. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AT205\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:24. Amino acids 42 to 54 of SEQ ID NO:24 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 55. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the AT205\_1i protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AT205\_1i should be approximately 825 bp.

#### Protein "AT211 1i"

One protein of the present invention has been identified as protein "AT211\_1i". A partial cDNA clone encoding AT211\_1i was first isolated from a human adult blood (lymphocytes and dendritic cells, treated with mixed lymphocyte reaction) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AT211\_1i".

Applicants' methods identified clone AT211\_1i as encoding a secreted 15 protein.

The nucleotide sequence of AT211\_1i as presently determined is reported in SEQ ID NO:25, and includes the poly(A) tail. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AT211\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:26.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AT211\_1i should be approximately 1100 bp.

#### Protein "AT319 1i"

20

One protein of the present invention has been identified as protein "AT319\_1i". A partial cDNA clone encoding AT319\_1i was first isolated from a human adult blood (lymphocytes and dendritic cells, treated with mixed lymphocyte reaction) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the LM.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR. This full-length clone

is also referred to herein as "AT319\_1i".

Applicants' methods identified clone AT319\_1i as encoding a secreted protein.

The nucleotide sequence of the 5' portion of AT319\_1i as presently determined is reported in SEQ ID NO:27. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AT319\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:28. Additional nucleotide sequence from the 3' portion of AT319\_1i is reported in SEQ ID NO:29.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AT319\_1i should be approximately 1680 bp.

# Protein "AW191\_1i"

25

One protein of the present invention has been identified as protein "AW191\_1i". A partial cDNA clone encoding AW191\_1i was first isolated from a human adult ovary (PA-1 teratocarcinoma line, pool of retinoic-acid-treated, activin-treated, and untreated tissue) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AW191\_1i".

Applicants' methods identified clone AW191\_1i as encoding a secreted protein.

The nucleotide sequence of the 5' portion of AW191\_1i as presently determined is reported in SEQ ID NO:30. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AW191\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:31. Amino acids 5 to 17 of SEQ ID NO:31 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 18. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the AW191\_1i protein.

Additional nucleotide sequence from the 3' portion of AW191\_1i, including a poly(A) tail, is reported in SEQ ID NO:32.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AW191\_1i should be approximately 1300 bp.

5

## Protein "BB9\_1i"

One protein of the present invention has been identified as protein "BB9\_1i". A partial cDNA clone encoding BB9\_1i was first isolated from a human adult blood (peripheral blood mononuclear cells, TH1- or TH2-driven response) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "BB9\_1i".

Applicants' methods identified clone BB9\_1i as encoding a secreted protein.

20

The nucleotide sequence of the 5' portion of BB9\_1i as presently determined is reported in SEQ ID NO:33. What applicants believe is the proper reading frame and the predicted amino acid sequence of the BB9\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:34. Additional nucleotide sequence from the 3' portion of BB9\_1i, including a poly(A) tail, is reported in SEQ ID NO:35.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone BB9\_1i should be approximately 1080 bp.

# Protein "H617 1i"

30

One protein of the present invention has been identified as protein "H617\_1i". A partial cDNA clone encoding H617\_1i was first isolated from a human adult blood (peripheral blood mononuclear cells, treated with phytohemagglutinin, phorbol myristate acetate, and mixed ly cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as

encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "H617\_1i".

Applicants' methods identified clone H617\_1i as encoding a secreted 10 protein.

The nucleotide sequence of the 5' portion of H617\_1i as presently determined is reported in SEQ ID NO:36. What applicants believe is the proper reading frame and the predicted amino acid sequence of the H617\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:37. Additional nucleotide sequence from the 3' portion of H617\_1i, including a poly(A) tail, is reported in SEQ ID NO:38.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone H617\_1i should be approximately 1600 bp.

# 20 <u>Protein "K39 1i"</u>

One protein of the present invention has been identified as protein "K39\_1i". A partial cDNA clone encoding K39\_1i was first isolated from a mouse adult bone marrow (stromal line FCM-4) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "K39\_1i".

Applicants' methods identified clone K39\_1i as encoding a secreted protein.

The nucleotide sequence of the 5' portion of K39\_1i as presently determined is reported in SEQ ID NO:39. What applicants believe is the proper reading frame and the predicted amino acid sequence of the K39\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:40. Additional nucleotide sequence from the 3' portion of K39\_1i, including a poly(A) tail, is reported in SEQ ID NO:41.

# Protein "K640\_1i"

One protein of the present invention has been identified as protein "K640\_1i". A partial cDNA clone encoding K640\_1i was first isolated from a mouse adult bone marrow (stromal line FCM-4) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "K640\_1i".

Applicants' methods identified clone K640\_1i as encoding a secreted protein.

The nucleotide sequence of the 5' portion of K640\_1i as presently determined is reported in SEQ ID NO:42. What applicants believe is the proper reading frame and the predicted amino acid sequence of the K640\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:43. Additional nucleotide sequence from the 3' portion of K640\_1i, including a poly(A) tail, is reported in SEQ ID NO:44.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone K640\_1i should be approximately 2400 bp.

30

20

# Protein "AE402 1i"

One protein of the present invention has been identified as protein "AE402\_1i". A partial cDNA clone encoding AE402\_1i was first isolated from a mouse adult spleen (stimulated with concanavalin A and mixed with dendritic cells) cDNA

library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AE402\_1i".

Applicants' methods identified clone AE402\_1i as encoding a secreted protein.

The nucleotide sequence of AE402\_1i as presently determined is reported in SEQ ID NO:45, and includes the poly(A) tail. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AE402\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:46.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AE402\_1i should be approximately 1200 bp.

## Protein "AE610 1i"

10

15

One protein of the present invention has been identified as protein "AE610\_1i". A partial cDNA clone encoding AE610\_1i was first isolated from a mouse adult spleen (stimulated with concanavalin A and mixed with dendritic cells) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AE610\_1i".

Applicants' methods identified clone AE610\_1i as encoding a secreted protein.

The nucleotide sequence of the 5' portion of AE610\_1i as presently

determined is reported in SEQ ID NO:47. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AE610\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:48. Amino acids 75 to 87 of SEQ ID NO:48 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 88. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the AE610\_1i protein. Additional nucleotide sequence from the 3' portion of AE610\_1i, including a poly(A) tail, is reported in SEQ ID NO:49.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AE610\_1i should be approximately 950 bp.

# Protein "AH106 1i"

10

25

One protein of the present invention has been identified as protein

"AH106\_1i". A partial cDNA clone encoding AH106\_1i was first isolated from a mouse
fetal thymus cDNA library using methods which are selective for cDNAs encoding
secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or
transmembrane protein on the basis of computer analysis of the amino acid sequence of
the encoded protein. A human EST matching at least part of the nucleotide sequence of
this clone was identified by database searches. The human cDNA clone corresponding
to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a
distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor
was examined and determined to be a full-length clone, including a 5' end and 3' UTR,
including a poly(A) tail. This full-length clone is also referred to herein as "AH106\_1i".

Applicants' methods identified clone AH106\_1i as encoding a secreted protein.

The nucleotide sequence of AH106\_1i as presently determined is reported in SEQ ID NO:50, and includes the poly(A) tail. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AH106\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:51.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AH106\_1i should be approximately 500 bp.

# Protein "AH196\_1i"

One protein of the present invention has been identified as protein "AH196\_1i". A partial cDNA clone encoding AH196\_1i was first isolated from a mouse fetal thymus cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AH196\_1i".

Applicants' methods identified clone AH196\_1i as encoding a secreted protein.

The nucleotide sequence of the 5' portion of AH196\_1i as presently determined is reported in SEQ ID NO:52. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AH196\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:53. Additional nucleotide sequence from the 3' portion of AH196\_1i, including a poly(A) tail, is reported in SEQ ID NO:54.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AH196\_1i should be approximately 870 bp.

#### Protein "AI6 1i"

15

20

One protein of the present invention has been identified as protein "AI6\_1i". A partial cDNA clone encoding AI6\_1i was first isolated from a human adult blood (peripheral blood mononuclear cells, TH1- or TH2-driven response) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A)

tail. This full-length clone is also referred to herein as "AI6\_1i".

Applicants' methods identified clone AI6\_1i as encoding a secreted protein.

The nucleotide sequence of the 5' portion of Al6\_1i as presently determined is reported in SEQ ID NO:55. What applicants believe is the proper reading frame and the predicted amino acid sequence of the Al6\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:56. Additional nucleotide sequence from the 3' portion of Al6\_1i, including a poly(A) tail, is reported in SEQ ID NO:57.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AI6\_1i should be approximately 900 bp.

AI6\_1i protein was expressed in a Baculovirus expression system, and an expressed protein band of approximately 6 kDa detected in a membrane fraction using SDS polyacrylamide gel electrophoresis.

## Protein "AI13\_1i"

10

One protein of the present invention has been identified as protein "AJ13\_1i". A partial cDNA clone encoding AJ13\_1i was first isolated from a human adult testes cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AJ13\_1i".

Applicants' methods identified clone AJ13\_1i as encoding a secreted protein.

The nucleotide sequence of AJ13\_1i as presently determined is reported in SEQ ID NO:58, and includes the poly(A) tail. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AJ13\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:59.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AJ13\_1i should be approximately 1200 bp.

# Protein "AJ27 1i"

10

25

One protein of the present invention has been identified as protein "AJ27\_1i". A partial cDNA clone encoding AJ27\_1i was first isolated from a human adult testes cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AJ27\_1i".

Applicants' methods identified clone AJ27\_1i as encoding a secreted protein.

The nucleotide sequence of the 5' portion of AJ27\_1i as presently determined is reported in SEQ ID NO:60. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AJ27\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:61. Amino acids 15 to 27 of SEQ ID NO:61 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 28. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the AJ27\_1i protein. Additional nucleotide sequence from the 3' portion of AJ27\_1i, including a poly(A) tail, is reported in SEQ ID NO:62.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AJ27\_1i should be approximately 1500 bp.

## Protein "AI142\_1i"

One protein of the present invention has been identified as protein "AJ142\_1i". A partial cDNA clone encoding AJ142\_1i was first isolated from a human adult testes cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of

this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AJ142\_1i".

Applicants' methods identified clone AJ142\_1i as encoding a secreted protein.

The nucleotide sequence of AJ142\_1i as presently determined is reported in SEQ ID NO:63, and includes the poly(A) tail. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AJ142\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:64. Amino acids 11 to 23 of SEQ ID NO:64 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 24. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the AJ142\_1i protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AJ142\_1i should be approximately 650 bp.

# 20 Protein "AK604 1i"

One protein of the present invention has been identified as protein "AK604\_1i". A partial cDNA clone encoding AK604\_1i was first isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AK604\_1i".

Applicants' methods identified clone AK604\_1i as encoding a secreted protein.

The nucleotide sequence of the 5' portion of AK604\_1i as presently

determined is reported in SEQ ID NO:65. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AK604\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:66. Additional nucleotide sequence from the 3' portion of AK604\_1i, including a poly(A) tail, is reported in SEQ ID NO:67.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AK604\_1i should be approximately 1350 bp.

#### Protein "AK620 1i"

One protein of the present invention has been identified as protein "AK620\_1i". A partial cDNA clone encoding AK620\_1i was first isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AK620\_1i".

Applicants' methods identified clone AK620\_1i as encoding a secreted protein.

The nucleotide sequence of AK620\_1i as presently determined is reported in SEQ ID NO:68, and includes the poly(A) tail. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AK620\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:69.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AK620\_1i should be approximately 700 bp.

# 30 Protein "AK650 Ti"

One protein of the present invention has been identified as protein "AK650\_1i". A partial cDNA clone encoding AK650\_1i was first isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or

transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AK650\_1i".

Applicants' methods identified clone AK650\_1i as encoding a secreted protein.

The nucleotide sequence of AK650\_1i as presently determined is reported in SEQ ID NO:70, and includes the poly(A) tail. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AK650\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:71. Amino acids 14 to 26 of SEQ ID NO:71 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 27. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the AK650\_1i protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AK650\_1i should be approximately 1000 bp.

## Protein "AM226 1i"

10

15

One protein of the present invention has been identified as protein "AM226\_1i". A partial cDNA clone encoding AM226\_1i was first isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AM226\_1i".

Applicants' methods identified clone AM226\_1i as encoding a secreted

protein.

30

The nucleotide sequence of the 5' portion of AM226\_1i as presently determined is reported in SEQ ID NO:72. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AM226\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:73. Amino acids 7 to 19 of SEQ ID NO:73 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 20. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the AM226\_1i protein. Additional nucleotide sequence from the 3' portion of AM226\_1i, including a poly(A) tail, is reported in SEQ ID NO:74.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AM226\_1i should be approximately 1500 bp.

AM226\_1i protein was expressed in a Baculovirus expression system, and
an expressed protein band of approximately 50 kDa detected in a conditioned medium fraction using SDS polyacrylamide gel electrophoresis.

# Protein "AR417 1i"

One protein of the present invention has been identified as protein "AR417\_1i". A partial cDNA clone encoding AR417\_1i was first isolated from a human adult retina cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AR417\_1i".

Applicants' methods identified clone AR417\_1i as encoding a secreted protein.

The nucleotide sequence of AR417\_1i as presently determined is reported in SEQ ID NO:75, and includes the poly(A) tail. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AR417\_1i protein

corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:76. Amino acids 32 to 44 of SEQ ID NO:76 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 45. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the AR417\_1i protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AR417\_1i should be approximately 1500 bp.

# 10 <u>Protein "AU43\_1i"</u>

15

20

One protein of the present invention has been identified as protein "AU43\_1i". A partial cDNA clone encoding AU43\_1i was first isolated from a human adult testes cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AU43\_1i".

Applicants' methods identified clone AU43\_1i as encoding a secreted protein.

25 determined is reported in SEQ ID NO:77. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AU43\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:78. Amino acids 11 to 23 of SEQ ID NO:78 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 24. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the AU43\_1i protein. Additional nucleotide sequence from the 3' portion of AU43\_1i, including a poly(A) tail, is reported in SEQ ID NO:79.

The EcoRI/NotI restriction fragment obtainable from the deposit

containing clone AU43\_1i should be approximately 950 bp.

## Protein "AW60 1i"

One protein of the present invention has been identified as protein

"AW60\_1i". A partial cDNA clone encoding AW60\_1i was first isolated from a human adult ovary (PA-1 teratocarcinoma line, pool of retinoic-acid-treated, activin-treated, and untreated tissue) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AW60\_1i".

Applicants' methods identified clone AW60\_1i as encoding a secreted protein.

The nucleotide sequence of the 5' portion of AW60\_1i as presently determined is reported in SEQ ID NO:80. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AW60\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:81. Amino acids 19 to 31 of SEQ ID NO:81 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 32. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the AW60\_1i protein. Additional nucleotide sequence from the 3' portion of AW60\_1i, including a poly(A) tail, is reported in SEQ ID NO:82.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AW60\_1i should be approximately 1800 bp.

30

# Protein "BA176 1i"

One protein of the present invention has been identified as protein "BA176\_1i". A partial cDNA clone encoding BA176\_1i was first isolated from a human fetal placenta cDNA library using methods which are selective for cDNAs encoding

secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "BA176\_1i".

Applicants' methods identified clone BA176\_1i as encoding a secreted 10 protein.

The nucleotide sequence of BA176\_1i as presently determined is reported in SEQ ID NO:83, and includes the poly(A) tail. What applicants believe is the proper reading frame and the predicted amino acid sequence of the BA176\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:84. Amino acids 276 to 288 of SEQ ID NO:84 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 289. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the BA176\_1i protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone BA176\_1i should be approximately 2500 bp.

## Protein "BD140 1i"

One protein of the present invention has been identified as protein "BD140\_1i". A partial cDNA clone encoding BD140\_1i was first isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "BD140\_1i".

Applicants' methods identified clone BD140\_1i as encoding a secreted protein.

The nucleotide sequence of BD140\_1i as presently determined is reported in SEQ ID NO:85, and includes the poly(A) tail. What applicants believe is the proper reading frame and the predicted amino acid sequence of the BD140\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:86.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone BD140\_1i should be approximately 2550 bp.

# Protein "BD407\_1i"

10

One protein of the present invention has been identified as protein "BD407\_1i". A partial cDNA clone encoding BD407\_1i was first isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "BD407\_1i".

Applicants' methods identified clone BD407\_1i as encoding a secreted protein.

The nucleotide sequence of BD407\_1i as presently determined is reported in SEQ ID NO:87, and includes the poly(A) tail. What applicants believe is the proper reading frame and the predicted amino acid sequence of the BD407\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:88. Amino acids 2 to 14 of SEQ ID NO:88 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 15. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the BD407\_1i protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone BD407\_1i should be approximately 1100 bp.

#### Protein "BF290 1i"

One protein of the present invention has been identified as protein "BF290\_1i". A partial cDNA clone encoding BF290\_1i was first isolated from a human fetal brain cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "BF290\_1i".

Applicants' methods identified clone BF290\_1i as encoding a secreted protein.

The nucleotide sequence of BF290\_1i as presently determined is reported in SEQ ID NO:89, and includes the poly(A) tail. What applicants believe is the proper reading frame and the predicted amino acid sequence of the BF290\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:90.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone BF290\_1i should be approximately 1450 bp.

# Protein "BG236\_1i"

15

20

25

One protein of the present invention has been identified as protein "BG236\_1i". A partial cDNA clone encoding BG236\_1i was first isolated from a human adult brain cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "BG236\_1i".

Applicants' methods identified clone BG236\_1i as encoding a secreted protein.

The nucleotide sequence of BG236\_1i as presently determined is reported in SEQ ID NO:91, and includes the poly(A) tail. What applicants believe is the proper reading frame and the predicted amino acid sequence of the BG236\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:92. Amino acids 45 to 57 of SEQ ID NO:92 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 58. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the BG236\_1i protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone BG236\_1i should be approximately 1350 bp.

#### Protein "BG237\_1i"

15

One protein of the present invention has been identified as protein "BG237\_1i". A partial cDNA clone encoding BG237\_1i was first isolated from a human adult brain cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "BG237\_1i".

Applicants' methods identified clone BG237\_1i as encoding a secreted protein.

The nucleotide sequence of the 5' portion of BG237\_1i as presently determined is reported in SEQ ID NO:93. What applicants believe is the proper reading frame and the predicted amino acid sequence of the BG237\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:94. Additional nucleotide sequence from the 3' portion of BG237\_1i, including a poly(A) tail, is reported in SEQ ID NO:95.

PCT/US99/31005 WO 00/37630

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone BG237\_1i should be approximately 1300 bp.

# Protein "BG255\_1i"

5

One protein of the present invention has been identified as protein "BG255\_1i". A partial cDNA clone encoding BG255\_1i was first isolated from a human adult brain cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of 10 the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, 15 including a poly(A) tail. This full-length clone is also referred to herein as "BG255\_1i".

Applicants' methods identified clone BG255\_1i as encoding a secreted protein.

The nucleotide sequence of the 5' portion of BG255\_1i as presently determined is reported in SEQ ID NO:96. What applicants believe is the proper reading frame and the predicted amino acid sequence of the BG255\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:97. Additional nucleotide sequence from the 3' portion of BG255\_1i, including a poly(A) tail, is reported in SEQ ID NO:98.

The EcoRI/NotI restriction fragment obtainable from the deposit 25 containing clone BG255\_1i should be approximately 1450 bp.

# <u> Protein "H541\_3i"</u>

One protein of the present invention has been identified as protein "H541\_3i". A partial cDNA clone encoding H541\_3i was first isolated from a human adult blood (peripheral blood mononuclear cells treated with phytohemagglutinin and phorbol myristate acetate and mixed I cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide

sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "H541\_3i".

Applicants' methods identified clone H541\_3i as encoding a secreted protein.

The nucleotide sequence of H541\_3i as presently determined is reported in SEQ ID NO:99, and includes the poly(A) tail. What applicants believe is the proper reading frame and the predicted amino acid sequence of the H541\_3i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:100. Amino acids 4 to 16 of SEQ ID NO:100 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 17. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the H541\_3i protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone H541\_3i should be approximately 1500 bp.

H541\_3i protein was expressed in a COS cell expression system, and an expressed protein band of approximately 41 kDa detected in a membrane fraction using SDS polyacrylamide gel electrophoresis.

# Protein "H978\_1i"

20

One protein of the present invention has been identified as protein "H978\_1i". A partial cDNA clone encoding H978\_1i was first isolated from a human adult blood (peripheral blood mononuclear cells treated with phytohemagglutinin and phorbol myristate acetate and mixed l cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from

PCT/US99/31005 WO 00/37630

the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR , including a poly(A) tail. This full-length clone is also referred to herein as "H978\_1i".

Applicants' methods identified clone H978\_1i as encoding a secreted prótein.

The nucleotide sequence of the 5' portion of H978\_1i as presently determined is reported in SEQ ID NO:101. What applicants believe is the proper reading frame and the predicted amino acid sequence of the H978\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:102. Additional nucleotide sequence from the 3' portion of H978\_1i, including a poly(A) tail, is reported in SEQ ID NO:103.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone H978\_1i should be approximately 1100 bp.

#### 15 Protein "L161\_1i"

25

One protein of the present invention has been identified as protein "L161\_1i". A partial cDNA clone encoding L161\_1i was first isolated from a mouse adult thymus cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or 20 transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "L161\_1i".

Applicants' methods identified clone L161\_1i as encoding a secreted protein.

The nucleotide sequence of the 5' portion of L161\_1i as presently determined is reported in SEQ ID NO:104. What applicants believe is the proper reading frame and the predicted amino acid sequence of the L161\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:105. Additional nucleotide sequence from the 3' portion of L161\_1i, including a poly(A) tail, is reported in SEQ ID NO:106.

The EcoRI/Notl restriction fragment obtainable from the deposit containing clone L161\_1i should be approximately 1300 bp.

## Protein "AE648\_1i"

One protein of the present invention has been identified as protein "AE648\_1i". A partial cDNA clone encoding AE648\_1i was first isolated from a mouse adult spleen (stimulated with concanavalin A and mixed with dendritic cells) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AE648\_1i".

Applicants' methods identified clone AE648\_1i as encoding a secreted protein.

The nucleotide sequence of AE648\_1i as presently determined is reported in SEQ ID NO:107, and includes the poly(A) tail. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AE648\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:108. Amino acids 3 to 15 of SEQ ID NO:108 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 16. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the AE648\_1i protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AE648\_1i should be approximately 900 bp.

30

5

15

## Protein "AE693 1i"

One protein of the present invention has been identified as protein "AE693\_1i". A partial cDNA clone encoding AE693\_1i was first isolated from a mouse adult spleen (stimulated with concanavalin A and mixed with dendritic cells) cDNA

library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AE693\_1i".

Applicants' methods identified clone AE693\_1i as encoding a secreted protein.

The nucleotide sequence of the 5' portion of AE693\_1i as presently determined is reported in SEQ ID NO:109. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AE693\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:110. Additional nucleotide sequence from the 3' portion of AE693\_1i, including a poly(A) tail, is reported in SEQ ID NO:111.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AE693\_1i should be approximately 1200 bp.

20

30

10

15

# Protein "AK438 1i"

One protein of the present invention has been identified as protein "AK438\_1i". A partial cDNA clone encoding AK438\_1i was first isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AK438\_1i".

Applicants' methods identified clone AK438\_1i as encoding a secreted protein.

The nucleotide sequence of the 5' portion of AK438\_1i as presently determined is reported in SEQ ID NO:112. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AK438\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:113. Additional nucleotide sequence from the 3' portion of AK438\_1i, including a poly(A) tail, is reported in SEQ ID NO:114.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AK438\_1i should be approximately 1000 bp.

# Protein "AK609 1i"

10

15

25

One protein of the present invention has been identified as protein "AK609\_1i". A partial cDNA clone encoding AK609\_1i was first isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR. This full-length clone is also referred to herein as "AK609\_1i".

Applicants' methods identified clone AK609\_1i as encoding a secreted protein.

The nucleotide sequence of the 5' portion of AK609\_1i as presently determined is reported in SEQ ID NO:115. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AK609\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:116. Additional nucleotide sequence from the 3' portion of AK609\_1i is reported in SEQ ID NO:117.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AK609\_1i should be approximately 750 bp.

#### Protein "AM1060\_1i"

One protein of the present invention has been identified as protein "AM1060\_1i". A partial cDNA clone encoding AM1060\_1i was first isolated from a human

fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AM1060\_1i".

Applicants' methods identified clone AM1060\_1i as encoding a secreted protein.

The nucleotide sequence of the 5' portion of AM1060\_1i as presently determined is reported in SEQ ID NO:118. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AM1060\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:119. Amino acids 13 to 25 of SEQ ID NO:119 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 26. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the AM1060\_1i protein. Additional nucleotide sequence from the 3' portion of AM1060\_1i, including a poly(A) tail, is reported in SEQ ID NO:120.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AM1060\_1i should be approximately 1700 bp.

# 25 Protein "AO2 1i"

10

One protein of the present invention has been identified as protein "AQ2\_1i". A partial cDNA clone encoding AQ2\_1i was first isolated from a human adult ovary (PA-1 teratocarcinoma line, pool of retinoic-acid-treated, activin-treated, and untreated tissue) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a

distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AQ2\_1i".

Applicants' methods identified clone AQ2\_1i as encoding a secreted 5 protein.

The nucleotide sequence of the 5' portion of AQ2\_1i as presently determined is reported in SEQ ID NO:121. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AQ2\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:122. Additional nucleotide sequence from the 3' portion of AQ2\_1i, including a poly(A) tail, is reported in SEQ ID NO:123.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AQ2\_1i should be approximately 1370 bp.

#### 15 <u>Protein "K433\_1i"</u>

30

One protein of the present invention has been identified as protein "K433\_1i". A partial cDNA clone encoding K433\_1i was first isolated from a mouse adult bone marrow (stromal line FCM-4) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "K433\_1i".

Applicants' methods identified clone K433\_1i as encoding a secreted protein.

The nucleotide sequence of the 5' portion of K433\_1i as presently determined is reported in SEQ ID NO:124. What applicants believe is the proper reading frame and the predicted amino acid sequence of the K433\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:125. Additional nucleotide sequence from the 3' portion of K433\_1i, including a poly(A) tail, is reported in SEQ ID

NO:126.

25

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone K433\_1i should be approximately 1200 bp.

## 5 <u>Protein "L256\_1i"</u>

One protein of the present invention has been identified as protein "L256\_1i". A partial cDNA clone encoding L256\_1i was first isolated from a mouse adult thymus cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "L256\_1i".

Applicants' methods identified clone L256\_1i as encoding a secreted protein.

The nucleotide sequence of the 5' portion of L256\_1i as presently determined is reported in SEQ ID NO:127. What applicants believe is the proper reading frame and the predicted amino acid sequence of the L256\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:128. Additional nucleotide sequence from the 3' portion of L256\_1i, including a poly(A) tail, is reported in SEQ ID NO:129.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone L256\_1i should be approximately 1400 bp.

## Protein "AM207\_1i"

One protein of the present invention has been identified as protein "AM207\_1i". A partial cDNA clone encoding AM207\_1i was first isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of

this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AM207\_1i".

Applicants' methods identified clone AM207\_1i as encoding a secreted protein.

The nucleotide sequence of the 5' portion of AM207\_1i as presently determined is reported in SEQ ID NO:130. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AM207\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:131. Additional nucleotide sequence from the 3' portion of AM207\_1i, including a poly(A) tail, is reported in SEQ ID NO:132.

#### Protein "AM910\_1i"

15

20

protein.

One protein of the present invention has been identified as protein "AM910\_1i". A partial cDNA clone encoding AM910\_1i was first isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AM910\_1i".

Applicants' methods identified clone AM910\_1i as encoding a secreted

The nucleotide sequence of AM910\_1i as presently determined is reported in SEQ ID NO:133, and includes the poly(A) tail. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AM910\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:134. Amino acids 7 to 19 of SEQ ID NO:134 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 20. Due to the

hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the AM910\_1i protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AM910\_1i should be approximately 1200 bp.

### Protein "AR54\_1i"

20

30

One protein of the present invention has been identified as protein "AR54\_1i". A partial cDNA clone encoding AR54\_1i was first isolated from a human adult retina cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AR54\_1i".

Applicants' methods identified clone AR54\_1i as encoding a secreted protein.

The nucleotide sequence of AR54\_1i as presently determined is reported in SEQ ID NO:135, and includes the poly(A) tail. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AR54\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:136.

25 Amino acids 8 to 20 of SEQ ID NO:136 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 21. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the AR54\_1i protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AR54\_1i should be approximately 1300 bp.

#### Protein "L200 1i"

One protein of the present invention has been identified as protein

"L200\_1i". A partial cDNA clone encoding L200\_1i was first isolated from a mouse adult thymus cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "L200\_1i".

Applicants' methods identified clone L200\_1i as encoding a secreted protein.

The nucleotide sequence of L200\_1i as presently determined is reported in SEQ ID NO:137, and includes the poly(A) tail. What applicants believe is the proper reading frame and the predicted amino acid sequence of the L200\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:138. Amino acids 272 to 284 of SEQ ID NO:138 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 285. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the L200\_1i protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone L200\_1i should be approximately 1330 bp.

### 25 Protein "WA129\_2i"

One protein of the present invention has been identified as protein "WA129\_2i". A partial cDNA clone encoding WA129\_2i was first isolated from a Xenopus embryo (dorsal mesoderm) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from

the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "WA129\_2i".

Applicants' methods identified clone WA129\_2i as encoding a secreted protein.

The nucleotide sequence of WA129\_2i as presently determined is reported in SEQ ID NO:139, and includes the poly(A) tail. What applicants believe is the proper reading frame and the predicted amino acid sequence of the WA129\_2i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:140.

Amino acids 10 to 22 of SEQ ID NO:140 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 23. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the WA129\_2i protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone WA129\_2i should be approximately 1933 bp.

WA192\_2i protein was expressed in a Baculovirus expression system, and an expressed protein band of approximately 39 kDa detected in a conditioned medium fraction using SDS polyacrylamide gel electrophoresis.

20

25

15

## Protein "WA154\_3i"

One protein of the present invention has been identified as protein "WA154\_3i". A partial cDNA clone encoding WA154\_3i was first isolated from a Xenopus embryo (dorsal mesoderm) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "WA154\_3i".

Applicants' methods identified clone WA154\_3i as encoding a secreted

protein.

10

20

25

The nucleotide sequence of WA154\_3i as presently determined is reported in SEQ ID NO:141, and includes the poly(A) tail. What applicants believe is the proper reading frame and the predicted amino acid sequence of the WA154\_3i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:142. Amino acids 11 to 23 of SEQ ID NO:142 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 24. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the WA154\_3i protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone WA154\_3i should be approximately 1469 bp.

WA154\_3i protein was expressed in a COS cell expression system, and an expressed protein band of approximately 17 kDa detected in conditioned medium and membrane fractions using SDS polyacrylamide gel electrophoresis.

### Protein "AA36\_1i"

One protein of the present invention has been identified as protein "AA36\_1i". A partial cDNA clone encoding AA36\_1i was first isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AA36\_1i".

Applicants' methods identified clone AA36\_1i as encoding a secreted 30 protein.

The nucleotide sequence of AA36\_1i as presently determined is reported in SEQ ID NO:143, and includes the poly(A) tail. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AA36\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:144.

Amino acids 3 to 15 of SEQ ID NO:144 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 16. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the AA36\_1i protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AA36\_1i should be approximately 1450 bp.

### Protein "AC175 2i"

One protein of the present invention has been identified as protein "AC175\_2i". A partial cDNA clone encoding AC175\_2i was first isolated from a human fetal placenta cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AC175\_2i".

Applicants' methods identified clone AC175\_2i as encoding a secreted protein.

The nucleotide sequence of AC175\_2i as presently determined is reported in SEQ ID NO:145, and includes the poly(A) tail. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AC175\_2i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:146.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone AC175\_2i should be approximately 842 bp.

#### <u> Protein "AV189\_1i"</u>

· 25

30

One protein of the present invention has been identified as protein "AV189\_1i". A partial cDNA clone encoding AV189\_1i was first isolated from a mouse adult spleen (concanavalin A stimulated and mixed with dendritic cells) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat.

No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "AV189\_1i".

Applicants' methods identified clone AV189\_1i as encoding a secreted protein.

The nucleotide sequence of AV189\_1i as presently determined is reported in SEQ ID NO:147, and includes the poly(A) tail. What applicants believe is the proper reading frame and the predicted amino acid sequence of the AV189\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:148. Amino acids 72 to 84 of SEQ ID NO:148 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 85. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the AV189\_1i protein.

20

25

10

15

## Protein "K368\_1i"

One protein of the present invention has been identified as protein "K368\_1i". A partial cDNA clone encoding K368\_1i was first isolated from a mouse adult bone marrow (stromal cell line FCM-4) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "K368\_1i".

Applicants' methods identified clone K368\_1i as encoding a secreted

protein.

10

15

30

The nucleotide sequence of K368\_1i as presently determined is reported in SEQ ID NO:149, and includes the poly(A) tail. What applicants believe is the proper reading frame and the predicted amino acid sequence of the K368\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:150. Amino acids 88 to 100 of SEQ ID NO:150 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 101. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the K368\_1i protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone K368\_1i should be approximately 983 bp.

K368\_1i protein was expressed in a Baculovirus expression system, and an expressed protein band of approximately 28 kDa detected in conditioned medium and membrane fractions using SDS polyacrylamide gel electrophoresis.

#### Protein "K568\_1i"

One protein of the present invention has been identified as protein "K568\_1i". A partial cDNA clone encoding K568\_1i was first isolated from a mouse adult bone marrow (stromal cell line FCM-4)cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "K568\_1i".

Applicants' methods identified clone K568\_1i as encoding a secreted protein.

The nucleotide sequence of K568\_1i as presently determined is reported in SEQ ID NO:151, and includes the poly(A) tail. What applicants believe is the proper reading frame and the predicted amino acid sequence of the K568\_1i protein

corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:152. Amino acids 57 to 69 of SEQ ID NO:152 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 70. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the K568\_1i protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone K568\_1i should be approximately 1254 bp.

### Protein "T85\_1i"

One protein of the present invention has been identified as protein "T85\_1i". A partial cDNA clone encoding T85\_1i was first isolated from a mouse fetal brain cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637),or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. A human EST matching at least part of the nucleotide sequence of this clone was identified by database searches. The human cDNA clone corresponding to the EST database entry was ordered from Genome Systems, Inc., St. Louis, Mo, a distributor of the I.M.A.G.E. Consortium library. The clone received from the distributor was examined and determined to be a full-length clone, including a 5' end and 3' UTR, including a poly(A) tail. This full-length clone is also referred to herein as "T85\_1i".

Applicants' methods identified clone T85\_1i as encoding a secreted protein.

The nucleotide sequence of T85\_1i as presently determined is reported in SEQ ID NO:153, and includes the poly(A) tail. What applicants believe is the proper reading frame and the predicted amino acid sequence of the T85\_1i protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:154.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone T85\_1i should be approximately 1803 bp.

#### 30

10

15

20

### Deposit of Clones

Clones AK296\_1i, AK533\_1i, AK583\_1i, AM282\_1i, AM340\_1i, AM610\_1i, AP162\_1i, AR260\_1i, AS32\_1i, AS34\_1i, AT205\_1i, AT211\_1i, AT319\_1i, AW191\_1i, BB9\_1i, H617\_1i, K39\_1i and K640\_1i were deposited on April 17, 1996 with the American

5

10

15

25

30

Type Culture Collection (10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and were given the accession number ATCC 98026, from which each clone comprising a particular polynucleotide is obtainable.

Clones AE402\_1i, AE610\_1i, AH106\_1i, AH196\_1i, AI6\_1i, AJ13\_1i, AJ27\_1i, AJ142\_1i, AK604\_1i, AK620\_1i, AK650\_1i, AM226\_1i, AR417\_1i, AU43\_1i, AW60\_1i, BA176\_1i, BD140\_1i, BD407\_1i and BF290\_1i were deposited on October 2, 1996 with the American Type Culture Collection (10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and were given the accession number ATCC 98190, from which each clone comprising a particular polynucleotide is obtainable.

Clones BG236\_1i, BG237\_1i, BG255\_1i, H541\_3i, H978\_1i and L161\_1i were deposited on October 2, 1996 with the American Type Culture Collection (10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and were given the accession number ATCC 98191, from which each clone comprising a particular polynucleotide is obtainable.

Clones AE648\_1i, AE693\_1i, AK438\_1i, AK609\_1i, AM1060\_1i, AQ2\_1i, K433\_1i and L256\_1i were deposited on October 31, 1996 with the American Type Culture Collection (10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and were given the accession number ATCC 98237, from which each clone comprising a particular polynucleotide is obtainable.

Clones AM207\_1i, AM910\_1i, AR54\_1i, L200\_1i, WA129\_2i and WA154\_3i were deposited on August 21, 1997 with the American Type Culture Collection (10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and were given the accession number ATCC 98510, from which each clone comprising a particular polynucleotide is obtainable.

Clones AA36\_1i, AC175\_2i, AV189\_1i, K368\_1i, K568\_1i and T85\_1i were deposited on December 18, 1998 with the American Type Culture Collection (10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and were given the accession number ATCC XXXXX, from which each clone comprising a particular polynucleotide is obtainable.

All restrictions on the availability to the public of the deposited material will be irrevocably removed upon the granting of the patent, except for the requirements specified in 37 C.F.R. § 1.808(b), and the term of the deposit will comply with 37 C.F.R.

§ 1.806.

10

15

20

25

30

Each clone has been transfected into separate bacterial cells (*E. coli*) in this composite deposit. Each clone can be removed from the vector in which it was deposited by performing an EcoRI/NotI digestion (5' site, EcoRI; 3' site, NotI) to produce the appropriate fragment for such clone. Each clone was deposited in either the pED6 or pNOTs vector depicted in Figures 1A and 1B, respectively. The pED6dpc2 vector ("pED6") was derived from pED6dpc1 by insertion of a new polylinker to facilitate cDNA cloning (Kaufman *et al.*, 1991, *Nucleic Acids Res.* 19: 4485-4490); the pNOTs vector was derived from pMT2 (Kaufman *et al.*, 1989, *Mol. Cell. Biol.* 9: 946-958) by deletion of the DHFR sequences, insertion of a new polylinker, and insertion of the M13 origin of replication in the ClaI site. In some instances, the deposited clone can become "flipped" (i.e., in the reverse orientation) in the deposited isolate. In such instances, the cDNA insert can still be isolated by digestion with EcoRI and NotI. However, NotI will then produce the 5' site and EcoRI will produce the 3' site for placement of the cDNA in proper orientation for expression in a suitable vector. The cDNA may also be expressed from the vectors in which they were deposited.

Bacterial cells containing a particular clone can be obtained from the composite deposit as follows:

An oligonucleotide probe or probes should be designed to the sequence that is known for that particular clone. This sequence can be derived from the sequences provided herein, or from a combination of those sequences.

In the probe sequences derived from the sequences provided, position 2 is occupied in preferred probes/primers by a biotinylated phosphoaramidite residue rather than a nucleotide (such as, for example, that produced by use of biotin p h o s p h o r a m i d i t e (1-dimethoxytrityloxy-2-(N-biotinyl-4-aminobutyl)-propyl-3-O-(2-cyanoethyl)-(N,N-dii sopropyl)-phosphoramadite) (Glen Research, cat. no. 10-1953)).

The design of the oligonucleotide probe should preferably follow these parameters:

- (a) It should be designed to an area of the sequence which has the fewest ambiguous bases ("N's"), if any;
- (b) It should be designed to have a  $T_m$  of approx. 80 ° C (assuming 2° for each A or T and 4 degrees for each G or C).

The oligonucleotide should preferably be labeled with -32P ATP (specific activity 6000 Ci/mmole) and T4 polynucleotide kinase using commonly employed techniques for labeling oligonucleotides. Other labeling techniques can also be used. Unincorporated label should preferably be removed by gel filtration chromatography or other established methods. The amount of radioactivity incorporated into the probe should be quantitated by measurement in a scintillation counter. Preferably, specific activity of the resulting probe should be approximately 4e+6 dpm/pmole.

The bacterial culture containing the pool of full-length clones should preferably be thawed and 100 l of the stock used to inoculate a sterile culture flask containing 25 ml of sterile L-broth containing ampicillin at 100 g/ml. The culture should preferably be grown to saturation at 37°C, and the saturated culture should preferably be diluted in fresh L-broth. Aliquots of these dilutions should preferably be plated to determine the dilution and volume which will yield approximately 5000 distinct and well-separated colonies on solid bacteriological media containing L-broth containing ampicillin at 100 g/ml and agar at 1.5% in a 150 mm petri dish when grown overnight at 37°C. Other known methods of obtaining distinct, well-separated colonies can also be employed.

15

20

Standard colony hybridization procedures should then be used to transfer the colonies to nitrocellulose filters and lyse, denature and bake them.

The filter is then preferably incubated at 65°C for 1 hour with gentle agitation in 6X SSC (20X stock is 175.3 g NaCl/liter, 88.2 g Na citrate/liter, adjusted to pH 7.0 with NaOH) containing 0.5% SDS, 100 g/ml of yeast RNA, and 10 mM EDTA (approximately 10 mL per 150 mm filter). Preferably, the probe is then added to the hybridization mix at a concentration greater than or equal to 1e+6 dpm/mL. The filter is then preferably incubated at 65°C with gentle agitation overnight. The filter is then preferably washed in 500 mL of 2X SSC/0.5% SDS at room temperature without agitation, preferably followed by 500 mL of 2X SSC/0.1% SDS at room temperature with gentle shaking for 15 minutes. A third wash with 0.1X SSC/0.5% SDS at 65°C for 30 minutes to 1 hour is optional. The filter is then preferably dried and subjected to autoradiography for sufficient time to visualize the positives on the X-ray film. Other known hybridization methods can also be employed.

The positive colonies are picked, grown in culture, and plasmid DNA isolated using standard procedures. The clones can then be verified by restriction analysis, hybridization analysis, or DNA sequencing.

Fragments of the proteins of the present invention which are capable of exhibiting biological activity are also encompassed by the present invention. Fragments of the protein may be in linear form or they may be cyclized using known methods, for example, as described in H.U. Saragovi, et al., Bio/Technology 10, 773-778 (1992) and in R.S. McDowell, et al., J. Amer. Chem. Soc. 114, 9245-9253 (1992), both of which are incorporated herein by reference. Such fragments may be fused to carrier molecules such as immunoglobulins for many purposes, including increasing the valency of protein binding sites. For example, fragments of the protein may be fused through "linker" sequences to the Fc portion of an immunoglobulin. For a bivalent form of the protein, such a fusion could be to the Fc portion of an IgG molecule. Other immunoglobulin isotypes may also be used to generate such fusions. For example, a protein - IgM fusion would generate a decayalent form of the protein of the invention.

The present invention also provides both full-length and mature forms of the disclosed proteins. The full-length form of the such proteins is identified in the sequence listing by translation of the nucleotide sequence of each disclosed clone. The mature form(s) of such protein may be obtained by expression of the disclosed full-length polynucleotide (preferably those deposited with ATCC) in a suitable mammalian cell or other host cell. The sequence(s) of the mature form(s) of the protein may also be determinable from the amino acid sequence of the full-length form.

15

20

30

Where the protein of the present invention is membrane-bound (e.g., is a receptor), the present invention also provides for soluble forms of such protein. In such forms, part or all of the intracellular and transmembrane domains of the protein are deleted such that the protein is fully secreted from the cell in which it is expressed. The intracellular and transmembrane domains of proteins of the invention can be identified in accordance with known techniques for determination of such domains from sequence information. For example, the TopPredII computer program can be used to predict the location of transmembrane domains in an amino acid sequence, domains which are described by the location of the center of the transmembrane domain, with at least ten transmembrane amino acids on each side of the reported central residue(s).

Proteins and protein fragments of the present invention include proteins with amino acid sequence lengths that are at least 25% (more preferably at least 50%, and most preferably at least 75%) of the length of a disclosed protein and have at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% or 95% identity) with that disclosed protein, where sequence identity is determined by

comparing the amino acid sequences of the proteins when aligned so as to maximize overlap and identity while minimizing sequence gaps. Also included in the present invention are proteins and protein fragments that contain a segment preferably comprising 8 or more (more preferably 20 or more, most preferably 30 or more) contiguous amino acids that shares at least 75% sequence identity (more preferably, at least 85% identity; most preferably at least 95% identity) with any such segment of any of the disclosed proteins.

In particular, sequence identity may be determined using WU-BLAST (Washington University BLAST) version 2.0 software, which builds upon WU-BLAST version 1.4, which in turn is based on the public domain NCBI-BLAST version 1.4 (Altschul and Gish, 1996, Local alignment statistics, Doolittle ed., Methods in Enzymology 266: 460-480; Altschul et al., 1990, Basic local alignment search tool, Journal of Molecular Biology 215: 403-410; Gish and States, 1993, Identification of protein coding regions by database similarity search, Nature Genetics 3: 266-272; Karlin and Altschul, 1993, Applications and statistics for multiple high-scoring segments in molecular sequences, Proc. Natl. Acad. Sci. USA 90: 5873-5877; all of which are incorporated by reference herein). WU-BLAST version 2.0 executable programs for several UNIX platforms can be downloaded from ftp://blast.wustl.edu/blast/executables. The complete suite of search programs (BLASTP, BLASTN, BLASTX, TBLASTN, and TBLASTX) is provided at that site, in addition to several support programs. WU-BLAST 2.0 is copyrighted and may not be sold or redistributed in any form or manner without the express written consent of the author; but the posted executables may otherwise be freely used for commercial, nonprofit, or academic purposes. In all search programs in the suite -- BLASTP, BLASTN, BLASTX, TBLASTN and TBLASTX -- the gapped alignment routines are integral to the database search itself, and thus yield much better sensitivity and selectivity while producing the more easily interpreted output. Gapping can optionally be turned off in all of these programs, if desired. The default penalty (Q) for a gap of length one is Q=9 for proteins and BLASTP, and Q=10 for BLASTN, but may be changed to any integer value including zero, one through eight, nine, ten, eleven, twelve through twenty, twenty-one through fifty, fifty-one through one hundred, etc. The default per-residue penalty for extending a gap (R) is R=2 for proteins and BLASTP, and R=10 for BLASTN, but may be changed to any integer value including zero, one, two, three, four, five, six,

20

25

10

20

25

seven, eight, nine, ten, eleven, twelve through twenty, twenty-one through fifty, fifty-one through one hundred, etc. Any combination of values for Q and R can be used in order to align sequences so as to maximize overlap and identity while minimizing sequence gaps. The default amino acid comparison matrix is BLOSUM62, but other amino acid comparison matrices such as PAM can be utilized.

Species homologues of the disclosed proteins are also provided by the present invention. As used herein, a "species homologue" is a protein or polynucleotide with a different species of origin from that of a given protein or polynucleotide, but with significant sequence similarity to the given protein or polynucleotide. Preferably, polynucleotide species homologues have at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% identity) with the given polynucleotide, and protein species homologues have at least 30% sequence identity (more preferably, at least 45% identity; most preferably at least 60% identity) with the given protein, where sequence identity is determined by comparing the nucleotide sequences of the polynucleotides or the amino acid sequences of the proteins when aligned so as to maximize overlap and identity while minimizing sequence gaps. Species homologues may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source from the desired species. Preferably, species homologues are those isolated from mammalian species. Most preferably, species homologues are those isolated from certain mammalian species such as, for example, Pan troglodytes, Gorilla gorilla, Pongo pygmaeus, Hylobates concolor, Macaca mulatta, Papio papio, Papio hamadryas, Cercopithecus aethiops, Cebus capucinus, Aotus trivirgatus, Sanguinus oedipus, Microcebus murinus, Mus musculus, Rattus norvegicus, Cricetulus griseus, Felis catus, Mustela vison, Canis familiaris, Oryctolagus cuniculus, Bos taurus, Ovis aries, Sus scrofa, and Equus caballus, for which genetic maps have been created allowing the identification of syntenic relationships between the genomic organization of genes in one species and the genomic organization of the related genes in another species (O'Brien and Seuánez, 1988, Ann. Rev. Genet. 22: 323-351; O'Brien et al., 1993, Nature Genetics 3:103-112; Johansson et al., 1995, Genomics 25: 682-690; Lyons et al., 1997, Nature Genetics 15: 47-56; O'Brien et al., 1997, Trends in Genetics 13(10): 393-399; Carver and Stubbs, 1997, Genome Research 7:1123-1137; all of which are incorporated by reference herein).

The invention also encompasses allelic variants of the disclosed proteins;

that is, naturally-occurring alternative forms of the isolated proteins which are identical or have significantly similar sequences to those encoded by the disclosed polynucleotides. Preferably, allelic variants have at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% identity) with the given polynucleotide, where sequence identity is determined by comparing the nucleotide sequences of the polynucleotides when aligned so as to maximize overlap and identity while minimizing sequence gaps. Allelic variants may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source from individuals of the appropriate species.

The invention also includes polynucleotides with sequences complementary to those of the polynucleotides disclosed herein.

10

The isolated polynucleotide endcoing the protein of the invention may be operably linked to an expression control sequence such as the pMT2 or pED expression vectors disclosed in Kaufman *et al.*, Nucleic Acids Res. 19, 4485-4490 (1991), in order to produce the protein recombinantly. Many suitable expression control sequences are known in the art. General methods of expressing recombinant proteins are also known and are exemplified in R. Kaufman, Methods in Enzymology 185, 537-566 (1990). As defined herein "operably linked" means that the isolated polynucleotide of the invention and an expression control sequence are situated within a vector or cell in such a way that the proteir is expressed by a host cell which has been transformed (transfected) with the ligated polynucleotide/expression control sequence.

A number of types of cells may act as suitable host cells for expression of the protein. Mammalian host cells include, for example, monkey COS cells, Chinese Hamster Ovary (CHO) cells, human kidney 293 cells, human epidermal A431 cells, human Colo205 cells, 3T3 cells, CV-1 cells, other transformed primate cell lines, normal diploid cells, cell strains derived from in vitro culture of primary tissue, primary explants, HeLa cells, mouse L cells, BHK, HL-60, U937, HaK or Jurkat cells.

Alternatively, it may be possible to produce the protein in lower eukaryotes such as yeast or in prokaryotes such as bacteria. Potentially suitable yeast strains include Saccharomyces cerevisiae, Schizosaccharomyces pombe, Kluyveromyces strains, Candida, or any yeast strain capable of expressing heterologous proteins. Potentially suitable bacterial strains include Escherichia coli, Bacillus subtilis, Salmonella typhimurium, or any bacterial strain capable of expressing heterologous proteins. If the protein is made in yeast or

5

bacteria, it may be necessary to modify the protein produced therein, for example by phosphorylation or glycosylation of the appropriate sites, in order to obtain the functional protein. Such covalent attachments may be accomplished using known chemical or enzymatic methods.

The protein may also be produced by operably linking the isolated polynucleotide of the invention to suitable control sequences in one or more insect expression vectors, and employing an insect expression system. Materials and methods for baculovirus/insect cell expression systems are commercially available in kit form from, e.g., Invitrogen, San Diego, California, U.S.A. (the MaxBac® kit), and such methods are well known in the art, as described in Summers and Smith, Texas Agricultural Experiment Station Bulletin No. 1555 (1987), incorporated herein by reference. As used herein, an insect cell capable of expressing a polynucleotide of the present invention is "transformed."

The protein of the invention may be prepared by culturing transformed host cells under culture conditions suitable to express the recombinant protein. The resulting expressed protein may then be purified from such culture (i.e., from culture medium or cell extracts) using known purification processes, such as gel filtration and ion exchange chromatography. The purification of the protein may also include an affinity column containing agents which will bind to the protein; one or more column steps over such affinity resins as concanavalin A-agarose, heparin-toyopearl® or Cibacrom blue 3GA Sepharose®; one or more steps involving hydrophobic interaction chromatography using such resins as phenyl ether, butyl ether, or propyl ether; or immunoaffinity chromatography.

Alternatively, the protein of the invention may also be expressed in a form which will facilitate purification. For example, it may be expressed as a fusion protein, such as those of maltose binding protein (MBP), glutathione-S-transferase (GST) or thioredoxin (TRX). Kits for expression and purification of such fusion proteins are commercially available from New England BioLabs (Beverly, MA), Pharmacia (Piscataway, NJ) and Invitrogen Corporation (Carlsbad, CA), respectively. The protein can also be tagged with an epitope and subsequently purified by using a specific antibody directed to such epitope. One such epitope ("Flag") is commercially available from the Eastman Kodak Company (New Haven, CT).

Finally, one or more reverse-phase high performance liquid chromatography (RP-HPLC) steps employing hydrophobic RP-HPLC media, e.g., silica

gel having pendant methyl or other aliphatic groups, can be employed to further purify the protein. Some or all of the foregoing purification steps, in various combinations, can also be employed to provide a substantially homogeneous isolated recombinant protein. The protein thus purified is substantially free of other mammalian proteins and is defined in accordance with the present invention as an "isolated protein."

The protein of the invention may also be expressed as a product of transgenic animals, e.g., as a component of the milk of transgenic cows, goats, pigs, or sheep which are characterized by somatic or germ cells containing a nucleotide sequence encoding the protein.

10

15

The protein may also be produced by known conventional chemical synthesis. Methods for constructing the proteins of the present invention by synthetic means are known to those skilled in the art. The synthetically-constructed protein sequences, by virtue of sharing primary, secondary or tertiary structural and/or conformational characteristics with proteins may possess biological properties in common therewith, including protein activity. Thus, they may be employed as biologically active or immunological substitutes for natural, purified proteins in screening of therapeutic compounds and in immunological processes for the development of antibodies.

The proteins provided herein also include proteins characterized by amino acid sequences similar to those of purified proteins but into which modification are naturally provided or deliberately engineered. For example, modifications in the peptide or DNA sequences can be made by those skilled in the art using known techniques. Modifications of interest in the protein sequences may include the alteration, substitution, replacement, insertion or deletion of a selected amino acid residue in the coding sequence. For example, one or more of the cysteine residues may be deleted or replaced with another amino acid to alter the conformation of the molecule. Techniques for such alteration, substitution, replacement, insertion or deletion are well known to those skilled in the art (see, e.g., U.S. Patent No. 4,518,584). Preferably, such alteration, substitution, replacement, insertion or deletion retains the desired activity of the protein.

Other fragments and derivatives of the sequences of proteins which would be expected to retain protein activity in whole or in part and may thus be useful for screening or other immunological methodologies may also be easily made by those skilled in the art given the disclosures herein. Such modifications are believed to be encompassed by the present invention.

PCT/US99/31005 WO 00/37630

#### **USES AND BIOLOGICAL ACTIVITY**

The proteins of the present invention are expected to exhibit one or more of the uses or biological activities (including those associated with assays cited herein) identified below. Uses or activities described for proteins of the present invention may be provided by administration or use of such proteins or by administration or use of polynucleotides encoding such proteins (such as, for example, in gene therapies or vectors suitable for introduction of DNA).

#### Research Uses and Utilities

10 The proteins provided by the present invention can similarly be used in assay to determine biological activity, including in a panel of multiple proteins for high-throughput screening; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in assays designed to quantitatively determine levels of the protein (or its receptor) in biological fluids; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state); and, of course, to isolate correlative receptors or ligands. Where the protein binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the protein can be used to identify the other protein with which binding occurs or to identify inhibitors of the binding interaction. Proteins involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.

Any or all of these research utilities are capable of being developed into reagent grade or kit format for commercialization as research products.

25 Methods for performing the uses listed above are well known to those skilled in the art. References disclosing such methods include without limitation "Molecular Cloning: A Laboratory Manual", 2d ed., Cold Spring Harbor Laboratory Press, Sambrook, J., E.F. Fritsch and T. Maniatis eds., 1989, and "Methods in Enzymology: Guide to Molecular Cloning Techniques", Academic Press, Berger, S.L. and A.R. Kimmel eds., 1987.

#### Nutritional Uses

30

Proteins of the present invention can also be used as nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid

supplement, use as a carbon source, use as a nitrogen source and use as a source of carbohydrate. In such cases the protein of the invention can be added to the feed of a particular organism or can be administered as a separate solid or liquid preparation, such as in the form of powder, pills, solutions, suspensions or capsules. In the case of microorganisms, the protein of the invention can be added to the medium in or on which the microorganism is cultured.

## Cytokine and Cell Proliferation/Differentiation Activity

A protein of the present invention may exhibit cytokine, cell proliferation (either inducing or inhibiting) or cell differentiation (either inducing or inhibiting) activity or may induce production of other cytokines in certain cell populations. Many protein factors discovered to date, including all known cytokines, have exhibited activity in one or more factor-dependent cell proliferation assays, and hence the assays serve as a convenient confirmation of cytokine activity. The activity of a protein of the present invention is evidenced by any one of a number of routine factor dependent cell proliferation assays for cell lines including, without limitation, 32D, DA2, DA1G, T10, B9, B9/11, BaF3, MC9/G, M+ (preB M+), 2E8, RB5, DA1, 123, T1165, HT2, CTLL2, TF-1, Mo7e and CMK.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for T-cell or thymocyte proliferation include without limitation those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Bertagnolli et al., J. Immunol. 145:1706-1712, 1990; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Bertagnolli, et al., J. Immunol. 149:3778-3783, 1992; Bowman et al., J. Immunol. 152: 1756-1761, 1994.

Assays for cytokine production and/or proliferation of spleen cells, lymph node cells or thymocytes include, without limitation, those described in: Polyclonal T cell stimulation, Kruisbeek, A.M. and Shevach, E.M. In *Current Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 3.12.1-3.12.14, John Wiley and Sons, Toronto. 1994; and Measurement of mouse and human Interferon, Schreiber, R.D. In *Current Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 6.8.1-6.8.8, John Wiley and Sons, Toronto. 1994.

Assays for proliferation and differentiation of hematopoietic and

lymphopoietic cells include, without limitation, those described in: Measurement of Human and Murine Interleukin 2 and Interleukin 4, Bottomly, K., Davis, L.S. and Lipsky, P.E. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.3.1-6.3.12, John Wiley and Sons, Toronto. 1991; deVries et al., J. Exp. Med. 173:1205-1211, 1991; Moreau et al., Nature 336:690-692, 1988; Greenberger et al., Proc. Natl. Acad. Sci. U.S.A. 80:2931-2938, 1983; Measurement of mouse and human interleukin 6 - Nordan, R. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.6.1-6.6.5, John Wiley and Sons, Toronto. 1991; Smith et al., Proc. Natl. Acad. Sci. U.S.A. 83:1857-1861, 1986; Measurement of human Interleukin 11 - Bennett, F., Giannotti, J., Clark, S.C. and Turner, K.J. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.15.1 John Wiley and Sons, Toronto. 1991; Measurement of mouse and human Interleukin 9 - Ciarletta, A., Giannotti, J., Clark, S.C. and Turner, K.J. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.13.1, John Wiley and Sons. Toronto. 1991.

Assays for T-cell clone responses to antigens (which will identify, among others, proteins that affect APC-T cell interactions as well as direct T-cell effects by measuring proliferation and cytokine production) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function; Chapter 6, Cytokines and their cellular receptors; Chapter 7, Immunologic studies in Humans); Weinberger et al., Proc. Natl. Acad. Sci. USA 77:6091-6095, 1980; Weinberger et al., Eur. J. Immun. 11:405-411, 1981; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988.

### Immune Stimulating or Suppressing Activity

25

A protein of the present invention may also exhibit immune stimulating or immune suppressing activity, including without limitation the activities for which assays are described herein. A protein may be useful in the treatment of various immune deficiencies and disorders (including severe combined immunodeficiency (SCID)), e.g., in regulating (up or down) growth and proliferation of T and/or B lymphocytes, as well as effecting the cytolytic activity of NK cells and other cell populations. These immune deficiencies may be genetic or be caused by viral (e.g., HIV) as well as bacterial or fungal infections, or may result from autoimmune disorders. More specifically, infectious diseases causes by viral, bacterial, fungal or other infection may be treatable using a

protein of the present invention, including infections by HIV, hepatitis viruses, herpesviruses, mycobacteria, Leishmania spp., malaria spp. and various fungal infections such as candidiasis. Of course, in this regard, a protein of the present invention may also be useful where a boost to the immune system generally may be desirable, *i.e.*, in the treatment of cancer.

Autoimmune disorders which may be treated using a protein of the present invention include, for example, connective tissue disease, multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune thyroiditis, insulin dependent diabetes mellitis, myasthenia gravis, graft-versus-host disease and autoimmune inflammatory eye disease. Such a protein of the present invention may also to be useful in the treatment of allergic reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems. Other conditions, in which immune suppression is desired (including, for example, organ transplantation), may also be treatable using a protein of the present invention.

15

Using the proteins of the invention it may also be possible to regulate immune responses in a number of ways. Down regulation may be in the form of inhibiting or blocking an immune response already in progress or may involve preventing the induction of an immune response. The functions of activated T cells may be inhibited by suppressing T cell responses or by inducing specific tolerance in T cells, or both. Immunosuppression of T cell responses is generally an active, non-antigen-specific, process which requires continuous exposure of the T cells to the suppressive agent. Tolerance, which involves inducing non-responsiveness or anergy in T cells, is distinguishable from immunosuppression in that it is generally antigen-specific and persists after exposure to the tolerizing agent has ceased. Operationally, tolerance can be demonstrated by the lack of a T cell response upon reexposure to specific antigen in the absence of the tolerizing agent.

Down regulating or preventing one or more antigen functions (including without limitation B lymphocyte antigen functions (such as , for example, B7)), e.g., preventing high level lymphokine synthesis by activated T cells, will be useful in situations of tissue, skin and organ transplantation and in graft-versus-host disease (GVHD). For example, blockage of T cell function should result in reduced tissue destruction in tissue transplantation. Typically, in tissue transplants, rejection of the transplant is initiated through its recognition as foreign by T cells, followed by an immune

reaction that destroys the transplant. The administration of a molecule which inhibits or blocks interaction of a B7 lymphocyte antigen with its natural ligand(s) on immune cells (such as a soluble, monomeric form of a peptide having B7-2 activity alone or in conjunction with a monomeric form of a peptide having an activity of another B lymphocyte antigen (e.g., B7-1, B7-3) or blocking antibody), prior to transplantation can lead to the binding of the molecule to the natural ligand(s) on the immune cells without transmitting the corresponding costimulatory signal. Blocking B lymphocyte antigen function in this matter prevents cytokine synthesis by immune cells, such as T cells, and thus acts as an immunosuppressant. Moreover, the lack of costimulation may also be sufficient to anergize the T cells, thereby inducing tolerance in a subject. Induction of long-term tolerance by B lymphocyte antigen-blocking reagents may avoid the necessity of repeated administration of these blocking reagents. To achieve sufficient immunosuppression or tolerance in a subject, it may also be necessary to block the function of a combination of B lymphocyte antigens.

The efficacy of particular blocking reagents in preventing organ transplant rejection or GVHD can be assessed using animal models that are predictive of efficacy in humans. Examples of appropriate systems which can be used include allogeneic cardiac grafts in rats and xenogeneic pancreatic islet cell grafts in mice, both of which have been used to examine the immunosuppressive effects of CTLA4Ig fusion proteins *in vivo* as described in Lenschow *et al.*, Science 257:789-792 (1992) and Turka *et al.*, Proc. Natl. Acad. Sci USA, 89:11102-11105 (1992). In addition, murine models of GVHD (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 846-847) can be used to determine the effect of blocking B lymphocyte antigen function *in vivo* on the development of that disease.

15

25

Blocking antigen function may also be therapeutically useful for treating autoimmune diseases. Many autoimmune disorders are the result of inappropriate activation of T cells that are reactive against self tissue and which promote the production of cytokines and autoantibodies involved in the pathology of the diseases. Preventing the activation of autoreactive T cells may reduce or eliminate disease symptoms. Administration of reagents which block costimulation of T cells by disrupting receptor: ligand interactions of B lymphocyte antigens can be used to inhibit T cell activation and prevent production of autoantibodies or T cell-derived cytokines which may be involved in the disease process. Additionally, blocking reagents may induce antigen-specific tolerance of autoreactive T cells which could lead to long-term relief from

the disease. The efficacy of blocking reagents in preventing or alleviating autoimmune disorders can be determined using a number of well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune encephalitis, systemic lupus erythmatosis in MRL/lpr/lpr mice or NZB hybrid mice, murine autoimmune collagen arthritis, diabetes mellitus in NOD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 840-856).

Upregulation of an antigen function (preferably a B lymphocyte antigen function), as a means of up regulating immune responses, may also be useful in therapy. Upregulation of immune responses may be in the form of enhancing an existing immune response or eliciting an initial immune response. For example, enhancing an immune response through stimulating B lymphocyte antigen function may be useful in cases of viral infection. In addition, systemic viral diseases such as influenza, the common cold, and encephalitis might be alleviated by the administration of stimulatory forms of B lymphocyte antigens systemically.

15

Alternatively, anti-viral immune responses may be enhanced in an infected patient by removing T cells from the patient, costimulating the T cells *in vitro* with viral antigen- pulsed APCs either expressing a peptide of the present invention or together with a stimulatory form of a soluble peptide of the present invention and reintroducing the *in vitro* activated T cells into the patient. Another method of enhancing anti-viral immune responses would be to isolate infected cells from a patient, transfect them with a nucleic acid encoding a protein of the present invention as described herein such that the cells express all or a portion of the protein on their surface, and reintroduce the transfected cells into the patient. The infected cells would now be capable of delivering a costimulatory signal to, and thereby activate, T cells *in vivo*.

In another application, up regulation or enhancement of antigen function (preferably B lymphocyte antigen function) may be useful in the induction of tumor immunity. Tumor cells (e.g., sarcoma, melanoma, lymphoma, leukemia, neuroblastoma, carcinoma) transfected with a nucleic acid encoding at least one peptide of the present invention can be administered to a subject to overcome tumor-specific tolerance in the subject. If desired, the tumor cell can be transfected to express a combination of peptides. For example, tumor cells obtained from a patient can be transfected ex vivo with an expression vector directing the expression of a peptide having B7-2-like activity alone, or in conjunction with a peptide having B7-1-like activity and/or B7-3-like activity. The

transfected tumor cells are returned to the patient to result in expression of the peptides on the surface of the transfected cell. Alternatively, gene therapy techniques can be used to target a tumor cell for transfection *in vivo*.

The presence of the peptide of the present invention having the activity of a B lymphocyte antigen(s) on the surface of the tumor cell provides the necessary costimulation signal to T cells to induce a T cell mediated immune response against the transfected tumor cells. In addition, tumor cells which lack MHC class I or MHC class II molecules, or which fail to reexpress sufficient amounts of MHC class I or MHC class II molecules, can be transfected with nucleic acid encoding all or a portion of (e.g., a cytoplasmic-domain truncated portion) of an MHC class I chain protein and 2 microglobulin protein or an MHC class II chain protein and an MHC class II chain protein to thereby express MHC class I or MHC class II proteins on the cell surface. Expression of the appropriate class I or class II MHC in conjunction with a peptide having the activity of a B lymphocyte antigen (e.g., B7-1, B7-2, B7-3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which blocks expression of an MHC class II associated protein, such as the invariant chain, can also be cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject.

15

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for thymocyte or splenocyte cytotoxicity include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Herrmann et al., J. Immunol. 137:3494-3500, 1986; Bowmanet al., J. Virology 61:1992-1998; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., J. Virology 61:1992-1998; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al.,

Cellular Immunology 133:327-341, 1991; Brown et al., J. Immunol. 153:3079-3092, 1994.

Assays for T-cell-dependent immunoglobulin responses and isotype switching (which will identify, among others, proteins that modulate T-cell dependent antibody responses and that affect Th1/Th2 profiles) include, without limitation, those described in: Maliszewski, J. Immunol. 144:3028-3033, 1990; and Assays for B cell function: In vitro antibody production, Mond, J.J. and Brunswick, M. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 3.8.1-3.8.16, John Wiley and Sons, Toronto. 1994.

Mixed lymphocyte reaction (MLR) assays (which will identify, among others, proteins that generate predominantly Th1 and CTL responses) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., J. Immunol. 149:3778-3783, 1992.

Dendritic cell-dependent assays (which will identify, among others, proteins expressed by dendritic cells that activate naive T-cells) include, without limitation, those described in: Guery et al., J. Immunol. 134:536-544, 1995; Inaba et al., Journal of Experimental Medicine 173:549-559, 1991; Macatonia et al., Journal of Immunology 154:5071-5079, 1995; Porgador et al., Journal of Experimental Medicine 182:255-260, 1995; Nair et al., Journal of Virology 67:4062-4069, 1993; Huang et al., Science 264:961-965, 1994; Macatonia et al., Journal of Experimental Medicine 169:1255-1264, 1989; Bhardwaj et al., Journal of Clinical Investigation 94:797-807, 1994; and Inaba et al., Journal of Experimental Medicine 172:631-640, 1990.

25

Assays for lymphocyte survival/apoptosis (which will identify, among others, proteins that prevent apoptosis after superantigen induction and proteins that regulate lymphocyte homeostasis) include, without limitation, those described in: Darzynkiewicz et al., Cytometry 13:795-808, 1992; Gorczyca et al., Leukemia 7:659-670, 1993; Gorczyca et al., Cancer Research 53:1945-1951, 1993; Itoh et al., Cell 66:233-243, 1991; Zacharchuk, Journal of Immunology 145:4037-4045, 1990; Zamai et al., Cytometry 14:891-897, 1993; Gorczyca et al., International Journal of Oncology 1:639-648, 1992.

Assays for proteins that influence early steps of T-cell commitment and development include, without limitation, those described in: Antica et al., Blood

84:111-117, 1994; Fine et al., Cellular Immunology 155:111-122, 1994; Galy et al., Blood 85:2770-2778, 1995; Toki et al., Proc. Nat. Acad Sci. USA 88:7548-7551, 1991.

# Hematopoiesis Regulating Activity

A protein of the present invention may be useful in regulation of hematopoiesis and, consequently, in the treatment of myeloid or lymphoid cell deficiencies. Even marginal biological activity in support of colony forming cells or of factor-dependent cell lines indicates involvement in regulating hematopoiesis, e.g. in supporting the growth and proliferation of erythroid progenitor cells alone or in combination with other cytokines, thereby indicating utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to stimulate the production of erythroid precursors and/or erythroid cells; in supporting the growth and proliferation of myeloid cells such as granulocytes and monocytes/macrophages (i.e., traditional CSF activity) useful, for example, in conjunction with chemotherapy to prevent 15 or treat consequent myelo-suppression; in supporting the growth and proliferation of megakaryocytes and consequently of platelets thereby allowing prevention or treatment of various platelet disorders such as thrombocytopenia, and generally for use in place of or complimentary to platelet transfusions; and/or in supporting the growth and proliferation of hematopoietic stem cells which are capable of maturing to any and all of 20 the above-mentioned hematopoietic cells and therefore find therapeutic utility in various stem cell disorders (such as those usually treated with transplantation, including, without limitation, aplastic anemia and paroxysmal nocturnal hemoglobinuria), as well as in repopulating the stem cell compartment post irradiation/chemotherapy, either in-vivo or ex-vivo (i.e., in conjunction with bone marrow transplantation or with peripheral progenitor cell transplantation (homologous or heterologous)) as normal cells or genetically manipulated for gene therapy.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for proliferation and differentiation of various hematopoietic lines are cited above.

Assays for embryonic stem cell differentiation (which will identify, among others, proteins that influence embryonic differentiation hematopoiesis) include, without limitation, those described in: Johansson et al. Cellular Biology 15:141-151, 1995; Keller et al., Molecular and Cellular Biology 13:473-486, 1993; McClanahan et al., Blood

81:2903-2915, 1993.

Assays for stem cell survival and differentiation (which will identify, among others, proteins that regulate lympho-hematopoiesis) include, without limitation, those described in: Methylcellulose colony forming assays, Freshney, M.G. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 265-268, Wiley-Liss, Inc., New York, NY. 1994; Hirayama et al., Proc. Natl. Acad. Sci. USA 89:5907-5911, 1992; Primitive hematopoietic colony forming cells with high proliferative potential, McNiece, I.K. and Briddell, R.A. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 23-39, Wiley-Liss, Inc., New York, NY. 1994; Neben et al., Experimental Hematology 22:353-359, 1994; Cobblestone area forming cell assay, Ploemacher, R.E. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 1-21, Wiley-Liss, Inc., New York, NY. 1994; Long term bone marrow cultures in the presence of stromal cells, Spooncer, E., Dexter, M. and Allen, T. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 163-179, Wiley-Liss, Inc., New York, NY. 1994; Long term culture initiating cell assay, Sutherland, 15 H.J. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 139-162, Wiley-Liss, Inc., New York, NY. 1994.

#### Tissue Growth Activity

A protein of the present invention also may have utility in compositions used for bone, cartilage, tendon, ligament and/or nerve tissue growth or regeneration, as well as for wound healing and tissue repair and replacement, and in the treatment of burns, incisions and ulcers.

A protein of the present invention, which induces cartilage and/or bone growth in circumstances where bone is not normally formed, has application in the healing of bone fractures and cartilage damage or defects in humans and other animals. Such a preparation employing a protein of the invention may have prophylactic use in closed as well as open fracture reduction and also in the improved fixation of artificial joints. *De novo* bone formation induced by an osteogenic agent contributes to the repair of congenital, trauma induced, or oncologic resection induced craniofacial defects, and also is useful in cosmetic plastic surgery.

A protein of this invention may also be used in the treatment of periodontal disease, and in other tooth repair processes. Such agents may provide an environment to attract bone-forming cells, stimulate growth of bone-forming cells or induce differentiation of progenitors of bone-forming cells. A protein of the invention may also

5

10

25

be useful in the treatment of osteoporosis or osteoarthritis, such as through stimulation of bone and/or cartilage repair or by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes.

Another category of tissue regeneration activity that may be attributable to the protein of the present invention is tendon/ligament formation. A protein of the present invention, which induces tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and other animals. Such a preparation employing a tendon/ligament-like tissue inducing protein may have prophylactic use in preventing damage to tendon or ligament tissue, as well as use in the improved fixation of tendon or ligament to bone or other tissues, and in repairing defects to tendon or ligament tissue. De novo tendon/ligament-like tissue formation induced by a composition of the present invention contributes to the repair of congenital, trauma induced, or other tendon or ligament defects of other origin, and is also useful in cosmetic plastic surgery for attachment or repair of tendons or ligaments. The compositions of the present invention may provide an environment to attract tendon- or ligament-forming cells, stimulate growth of tendon- or ligament-forming cells, induce differentiation of progenitors of tendon- or ligament-forming cells, or induce growth of tendon/ligament cells or progenitors ex vivo for return in vivo to effect tissue repair. The compositions of the invention may also be useful in the treatment of tendinitis, carpal tunnel syndrome and other tendon or ligament defects. The compositions may also include an appropriate matrix and/or sequestering agent as a carrier as is well known in the art.

The protein of the present invention may also be useful for proliferation of neural cells and for regeneration of nerve and brain tissue, *i.e.* for the treatment of central and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders, which involve degeneration, death or trauma to neural cells or nerve tissue. More specifically, a protein may be used in the treatment of diseases of the peripheral nervous system, such as peripheral nerve injuries, peripheral neuropathy and localized neuropathies, and central nervous system diseases, such as Alzheimer's, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome. Further conditions which may be treated in accordance with the present invention include mechanical and traumatic disorders, such as spinal cord disorders, head

trauma and cerebrovascular diseases such as stroke. Peripheral neuropathies resulting from chemotherapy or other medical therapies may also be treatable using a protein of the invention.

Proteins of the invention may also be useful to promote better or faster closure of non-healing wounds, including without limitation pressure ulcers, ulcers associated with vascular insufficiency, surgical and traumatic wounds, and the like.

It is expected that a protein of the present invention may also exhibit activity for generation or regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac) and vascular (including vascular endothelium) tissue, or for promoting the growth of cells comprising such tissues. Part of the desired effects may be by inhibition or modulation of fibrotic scarring to allow normal tissue to regenerate. A protein of the invention may also exhibit angiogenic activity.

A protein of the present invention may also be useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokine damage.

A protein of the present invention may also be useful for promoting or inhibiting differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for tissue generation activity include, without limitation, those described in: International Patent Publication No. WO95/16035 (bone, cartilage, tendon); International Patent Publication No. WO95/05846 (nerve, neuronal); International Patent Publication No. WO91/07491 (skin, endothelium).

Assays for wound healing activity include, without limitation, those described in: Winter, Epidermal Wound Healing, pps. 71-112 (Maibach, HI and Rovee, DT, eds.), Year Book Medical Publishers, Inc., Chicago, as modified by Eaglstein and Mertz, J. Invest. Dermatol 71:382-84 (1978).

30

20

### Activin/Inhibin Activity

A protein of the present invention may also exhibit activin- or inhibin-related activities. Inhibins are characterized by their ability to inhibit the release of follicle stimulating hormone (FSH), while activins and are characterized by their ability

to stimulate the release of follicle stimulating hormone (FSH). Thus, a protein of the present invention, alone or in heterodimers with a member of the inhibin family, may be useful as a contraceptive based on the ability of inhibins to decrease fertility in female mammals and decrease spermatogenesis in male mammals. Administration of sufficient amounts of other inhibins can induce infertility in these mammals. Alternatively, the protein of the invention, as a homodimer or as a heterodimer with other protein subunits of the inhibin- group, may be useful as a fertility inducing therapeutic, based upon the ability of activin molecules in stimulating FSH release from cells of the anterior pituitary. See, for example, United States Patent 4,798,885. A protein of the invention may also be useful for advancement of the onset of fertility in sexually immature mammals, so as to increase the lifetime reproductive performance of domestic animals such as cows, sheep and pigs.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for activin/inhibin activity include, without limitation, those described in: Vale et al., Endocrinology 91:562-572, 1972; Ling et al., Nature 321:779-782, 1986; Vale et al., Nature 321:776-779, 1986; Mason et al., Nature 318:659-663, 1985; Forage et al., Proc. Natl. Acad. Sci. USA 83:3091-3095, 1986.

### 20 <u>Chemotactic/Chemokinetic Activity</u>

15

30

A protein of the present invention may have chemotactic or chemokinetic activity (e.g., act as a chemokine) for mammalian cells, including, for example, monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells. Chemotactic and chemokinetic proteins can be used to mobilize or attract a desired cell population to a desired site of action. Chemotactic or chemokinetic proteins provide particular advantages in treatment of wounds and other trauma to tissues, as well as in treatment of localized infections. For example, attraction of lymphocytes, monocytes or neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

A protein or peptide has chemotactic activity for a particular cell population if it can stimulate, directly or indirectly, the directed orientation or movement of such cell population. Preferably, the protein or peptide has the ability to directly stimulate directed movement of cells. Whether a particular protein has chemotactic activity for a population of cells can be readily determined by employing such protein or

peptide in any known assay for cell chemotaxis.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for chemotactic activity (which will identify proteins that induce or prevent chemotaxis) consist of assays that measure the ability of a protein to induce the migration of cells across a membrane as well as the ability of a protein to induce the adhesion of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W.Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 6.12, Measurement of alpha and beta Chemokines 6.12.1-6.12.28; Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al. APMIS 103:140-146, 1995; Muller et al Eur. J. Immunol. 25: 1744-1748; Gruber et al. J. of Immunol. 152:5860-5867, 1994; Johnston et al. J. of Immunol. 153: 1762-1768, 1994.

15

25

## Hemostatic and Thrombolytic Activity

A protein of the invention may also exhibit hemostatic or thrombolytic activity. As a result, such a protein is expected to be useful in treatment of various coagulation disorders (including hereditary disorders, such as hemophilias) or to enhance coagulation and other hemostatic events in treating wounds resulting from trauma, surgery or other causes. A protein of the invention may also be useful for dissolving or inhibiting formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as, for example, infarction of cardiac and central nervous system vessels (e.g., stroke).

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assay for hemostatic and thrombolytic activity include, without limitation, those described in: Linet et al., J. Clin. Pharmacol. 26:131-140, 1986; Burdick et al., Thrombosis Res. 45:413-419, 1987; Humphrey et al., Fibrinolysis 5:71-79 (1991); Schaub, Prostaglandins 35:467-474, 1988.

### Receptor/Ligand Activity

A protein of the present invention may also demonstrate activity as receptors, receptor ligands or inhibitors or agonists of receptor/ligand interactions.

Examples of such receptors and ligands include, without limitation, cytokine receptors and their ligands, receptor kinases and their ligands, receptor phosphatases and their ligands, receptors involved in cell-cell interactions and their ligands (including without limitation, cellular adhesion molecules (such as selectins, integrins and their ligands) and receptor/ligand pairs involved in antigen presentation, antigen recognition and development of cellular and humoral immune responses). Receptors and ligands are also useful for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. A protein of the present invention (including, without limitation, fragments of receptors and ligands) may themselves be useful as inhibitors of receptor/ligand interactions.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for receptor-ligand activity include without limitation those described in:Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W.Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 7.28, Measurement of Cellular Adhesion under static conditions 7.28.1-7.28.22), Takai et al., Proc. Natl. Acad. Sci. USA 84:6864-6868, 1987; Bierer et al., J. Exp. Med. 168:1145-1156, 1988; Rosenstein et al., J. Exp. Med. 169:149-160 1989; Stoltenborg et al., J. Immunol. Methods 175:59-68, 1994; Stitt et al., Cell 80:661-670, 1995.

#### Anti-Inflammatory Activity

10

20

Proteins of the present invention may also exhibit anti-inflammatory activity. The anti-inflammatory activity may be achieved by providing a stimulus to cells involved in the inflammatory response, by inhibiting or promoting cell-cell interactions (such as, for example, cell adhesion), by inhibiting or promoting chemotaxis of cells involved in the inflammatory process, inhibiting or promoting cell extravasation, or by stimulating or suppressing production of other factors which more directly inhibit or promote an inflammatory response. Proteins exhibiting such activities can be used to treat inflammatory conditions including chronic or acute conditions), including without limitation inflammation associated with infection (such as septic shock, sepsis or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine or chemokine-induced lung injury, inflammatory bowel disease, Crohn's disease or resulting

from over production of cytokines such as TNF or IL-1. Proteins of the invention may also be useful to treat anaphylaxis and hypersensitivity to an antigenic substance or material.

## Cadherin/Tumor Invasion Suppressor Activity

5

20

Cadherins are calcium-dependent adhesion molecules that appear to play major roles during development, particularly in defining specific cell types. Loss or alteration of normal cadherin expression can lead to changes in cell adhesion properties linked to tumor growth and metastasis. Cadherin malfunction is also implicated in other human diseases, such as pemphigus vulgaris and pemphigus foliaceus (auto-immune blistering skin diseases), Crohn's disease, and some developmental abnormalities.

The cadherin superfamily includes well over forty members, each with a distinct pattern of expression. All members of the superfamily have in common conserved extracellular repeats (cadherin domains), but structural differences are found in other parts of the molecule. The cadherin domains bind calcium to form their tertiary structure and thus calcium is required to mediate their adhesion. Only a few amino acids in the first cadherin domain provide the basis for homophilic adhesion; modification of this recognition site can change the specificity of a cadherin so that instead of recognizing only itself, the mutant molecule can now also bind to a different cadherin. In addition, some cadherins engage in heterophilic adhesion with other cadherins.

E-cadherin, one member of the cadherin superfamily, is expressed in epithelial cell types. Pathologically, if E-cadherin expression is lost in a tumor, the malignant cells become invasive and the cancer metastasizes. Transfection of cancer cell lines with polynucleotides expressing E-cadherin has reversed cancer-associated changes by returning altered cell shapes to normal, restoring cells' adhesiveness to each other and to their substrate, decreasing the cell growth rate, and drastically reducing anchorage-independent cell growth. Thus, reintroducing E-cadherin expression reverts carcinomas to a less advanced stage. It is likely that other cadherins have the same invasion suppressor role in carcinomas derived from other tissue types. Therefore, proteins of the present invention with cadherin activity, and polynucleotides of the present invention encoding such proteins, can be used to treat cancer. Introducing such proteins or polynucleotides into cancer cells can reduce or eliminate the cancerous changes observed in these cells by providing normal cadherin expression.

Cancer cells have also been shown to express cadherins of a different tissue type than their origin, thus allowing these cells to invade and metastasize in a different

tissue in the body. Proteins of the present invention with cadherin activity, and polynucleotides of the present invention encoding such proteins, can be substituted in these cells for the inappropriately expressed cadherins, restoring normal cell adhesive properties and reducing or eliminating the tendency of the cells to metastasize.

Additionally, proteins of the present invention with cadherin activity, and polynucleotides of the present invention encoding such proteins, can used to generate antibodies recognizing and binding to cadherins. Such antibodies can be used to block the adhesion of inappropriately expressed tumor-cell cadherins, preventing the cells from forming a tumor elsewhere. Such an anti-cadherin antibody can also be used as a marker for the grade, pathological type, and prognosis of a cancer, i.e. the more progressed the cancer, the less cadherin expression there will be, and this decrease in cadherin expression can be detected by the use of a cadherin-binding antibody.

Fragments of proteins of the present invention with cadherin activity, preferably a polypeptide comprising a decapeptide of the cadherin recognition site, and poly-nucleotides of the present invention encoding such protein fragments, can also be used to block cadherin function by binding to cadherins and preventing them from binding in ways that produce undesirable effects. Additionally, fragments of proteins of the present invention with cadherin activity, preferably truncated soluble cadherin fragments which have been found to be stable in the circulation of cancer patients, and polynucleotides encoding such protein fragments, can be used to disturb proper cell-cell adhesion.

Assays for cadherin adhesive and invasive suppressor activity include, without limitation, those described in: Hortsch et al. J Biol Chem 270 (32): 18809-18817, 1995; Miyaki et al. Oncogene 11: 2547-2552, 1995; Ozawa et al. Cell 63: 1033-1038, 1990.

25

5

## Tumor Inhibition Activity

In addition to the activities described above for immunological treatment or prevention of tumors, a protein of the invention may exhibit other anti-tumor activities. A protein may inhibit tumor growth directly or indirectly (such as, for example, via antibody-dependent cell-mediated cytotoxicity (ADCC)). A protein may exhibit its tumor inhibitory activity by acting on tumor tissue or tumor precursor tissue, by inhibiting formation of tissues necessary to support tumor growth (such as, for example, by inhibiting angiogenesis), by causing production of other factors, agents or cell types which inhibit tumor growth, or by suppressing, eliminating or inhibiting factors, agents or cell

types which promote tumor growth.

## Other Activities

A protein of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria, viruses, fungi and other parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, weight, hair color, eye color, skin, fat to lean ratio or other tissue pigmentation, or organ or body part size or shape (such as, for example, breast augmentation or diminution, change in bone form or shape); effecting biorhythms or caricadic cycles or rhythms; effecting the fertility of male or female subjects; effecting the metabolism, catabolism, anabolism, processing, utilization, storage or elimination of dietary fat, lipid, protein, carbohydrate, vitamins, minerals, cofactors or other nutritional factors or component(s); effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), depression (including depressive disorders) and violent behaviors; providing analgesic effects or other pain reducing effects; promoting differentiation and growth of embryonic stem cells in lineages other than hematopoietic lineages; hormonal or endocrine activity; in the case of enzymes, correcting deficiencies of the enzyme and treating deficiency-related diseases; treatment of hyperproliferative disorders (such as, for example, psoriasis); immunoglobulin-like activity (such as, for example, the ability to bind antigens or complement); and the ability to act as an antigen in a vaccine composition to raise an immune response against such protein or another material or entity which is cross-reactive with such protein.

25

15

## **ADMINISTRATION AND DOSING**

A protein of the present invention (from whatever source derived, including without limitation from recombinant and non-recombinant sources) may be used in a pharmaceutical composition when combined with a pharmaceutically acceptable carrier. Such a composition may also contain (in addition to protein and a carrier) diluents, fillers, salts, buffers, stabilizers, solubilizers, and other materials well known in the art. The term "pharmaceutically acceptable" means a non-toxic material that does not interfere with the effectiveness of the biological activity of the active ingredient(s). The characteristics of the carrier will depend on the route of administration. The

pharmaceutical composition of the invention may also contain cytokines, lymphokines, or other hematopoietic factors such as M-CSF, GM-CSF, TNF, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, IL-14, IL-15, IFN, TNF0, TNF1, TNF2, G-CSF, Meg-CSF, thrombopoietin, stem cell factor, and erythropoietin. The pharmaceutical composition may further contain other agents which either enhance the activity of the protein or compliment its activity or use in treatment. Such additional factors and/or agents may be included in the pharmaceutical composition to produce a synergistic effect with protein of the invention, or to minimize side effects. Conversely, protein of the present invention may be included in formulations of the particular cytokine, lymphokine, other hematopoietic factor, thrombolytic or anti-thrombotic factor, or anti-inflammatory agent to minimize side effects of the cytokine, lymphokine, other hematopoietic factor, thrombolytic or anti-inflammatory agent.

A protein of the present invention may be active in multimers (e.g., heterodimers or homodimers) or complexes with itself or other proteins. As a result, pharmaceutical compositions of the invention may comprise a protein of the invention in such multimeric or complexed form.

The pharmaceutical composition of the invention may be in the form of a complex of the protein(s) of present invention along with protein or peptide antigens. The protein and/or peptide antigen will deliver a stimulatory signal to both B and T lymphocytes. B lymphocytes will respond to antigen through their surface immunoglobulin receptor. T lymphocytes will respond to antigen through the T cell receptor (TCR) following presentation of the antigen by MHC proteins. MHC and structurally related proteins including those encoded by class I and class II MHC genes on host cells will serve to present the peptide antigen(s) to T lymphocytes. The antigen components could also be supplied as purified MHC-peptide complexes alone or with co-stimulatory molecules that can directly signal T cells. Alternatively antibodies able to bind surface immunolgobulin and other molecules on B cells as well as antibodies able to bind the TCR and other molecules on T cells can be combined with the pharmaceutical composition of the invention.

The pharmaceutical composition of the invention may be in the form of a liposome in which protein of the present invention is combined, in addition to other pharmaceutically acceptable carriers, with amphipathic agents such as lipids which exist in aggregated form as micelles, insoluble monolayers, liquid crystals, or lamellar layers in aqueous solution. Suitable lipids for liposomal formulation include, without limitation,

30

monoglycerides, diglycerides, sulfatides, lysolecithin, phospholipids, saponin, bile acids, and the like. Preparation of such liposomal formulations is within the level of skill in the art, as disclosed, for example, in U.S. Patent No. 4,235,871; U.S. Patent No. 4,501,728; U.S. Patent No. 4,837,028; and U.S. Patent No. 4,737,323, all of which are incorporated herein by reference.

As used herein, the term "therapeutically effective amount" means the total amount of each active component of the pharmaceutical composition or method that is sufficient to show a meaningful patient benefit, i.e., treatment, healing, prevention or amelioration of the relevant medical condition, or an increase in rate of treatment, healing, prevention or amelioration of such conditions. When applied to an individual active ingredient, administered alone, the term refers to that ingredient alone. When applied to a combination, the term refers to combined amounts of the active ingredients that result in the therapeutic effect, whether administered in combination, serially or simultaneously.

10

15

20

25

In practicing the method of treatment or use of the present invention, a therapeutically effective amount of protein of the present invention is administered to a mammal having a condition to be treated. Protein of the present invention may be administered in accordance with the method of the invention either alone or in combination with other therapies such as treatments employing cytokines, lymphokines or other hematopoietic factors. When co-administered with one or more cytokines, lymphokines or other hematopoietic factors, protein of the present invention may be administered either simultaneously with the cytokine(s), lymphokine(s), other hematopoietic factor(s), thrombolytic or anti-thrombotic factors, or sequentially. If administered sequentially, the attending physician will decide on the appropriate sequence of administering protein of the present invention in combination with cytokine(s), lymphokine(s), other hematopoietic factor(s), thrombolytic or anti-thrombotic factors.

Administration of protein of the present invention used in the pharmaceutical composition or to practice the method of the present invention can be carried out in a variety of conventional ways, such as oral ingestion, inhalation, topical application or cutaneous, subcutaneous, intraperitoneal, parenteral or intravenous injection. Intravenous administration to the patient is preferred.

When a therapeutically effective amount of protein of the present invention is administered orally, protein of the present invention will be in the form of a tablet, capsule, powder, solution or elixir. When administered in tablet form, the pharmaceutical

composition of the invention may additionally contain a solid carrier such as a gelatin or an adjuvant. The tablet, capsule, and powder contain from about 5 to 95% protein of the present invention, and preferably from about 25 to 90% protein of the present invention. When administered in liquid form, a liquid carrier such as water, petroleum, oils of animal or plant origin such as peanut oil, mineral oil, soybean oil, or sesame oil, or synthetic oils may be added. The liquid form of the pharmaceutical composition may further contain physiological saline solution, dextrose or other saccharide solution, or glycols such as ethylene glycol, propylene glycol or polyethylene glycol. When administered in liquid form, the pharmaceutical composition contains from about 0.5 to 90% by weight of protein of the present invention, and preferably from about 1 to 50% protein of the present invention.

When a therapeutically effective amount of protein of the present invention is administered by intravenous, cutaneous or subcutaneous injection, protein of the present invention will be in the form of a pyrogen-free, parenterally acceptable aqueous solution. The preparation of such parenterally acceptable protein solutions, having due regard to pH, isotonicity, stability, and the like, is within the skill in the art. A preferred pharmaceutical composition for intravenous, cutaneous, or subcutaneous injection should contain, in addition to protein of the present invention, an isotonic vehicle such as Sodium Chloride Injection, Ringer's Injection, Dextrose Injection, Dextrose and Sodium Chloride Injection, Lactated Ringer's Injection, or other vehicle as known in the art. The pharmaceutical composition of the present invention may also contain stabilizers, preservatives, buffers, antioxidants, or other additives known to those of skill in the art.

15

20

25

30

The amount of protein of the present invention in the pharmaceutical composition of the present invention will depend upon the nature and severity of the condition being treated, and on the nature of prior treatments which the patient has undergone. Ultimately, the attending physician will decide the amount of protein of the present invention with which to treat each individual patient. Initially, the attending physician will administer low doses of protein of the present invention and observe the patient's response. Larger doses of protein of the present invention may be administered until the optimal therapeutic effect is obtained for the patient, and at that point the dosage is not increased further. It is contemplated that the various pharmaceutical compositions used to practice the method of the present invention should contain about 0.01 g to about 100 mg (preferably about 0.1ng to about 10 mg, more preferably about 0.1 g to about 1 mg) of protein of the present invention per kg body weight.

The duration of intravenous therapy using the pharmaceutical composition of the present invention will vary, depending on the severity of the disease being treated and the condition and potential idiosyncratic response of each individual patient. It is contemplated that the duration of each application of the protein of the present invention will be in the range of 12 to 24 hours of continuous intravenous administration. Ultimately the attending physician will decide on the appropriate duration of intravenous therapy using the pharmaceutical composition of the present invention.

Protein of the invention may also be used to immunize animals to obtain polyclonal and monoclonal antibodies which specifically react with the protein. Such antibodies may be obtained using either the entire protein or fragments thereof as an immunogen. The peptide immunogens additionally may contain a cysteine residue at the carboxyl terminus, and are conjugated to a hapten such as keyhole limpet hemocyanin (KLH). Methods for synthesizing such peptides are known in the art, for example, as in R.P. Merrifield, J. Amer.Chem.Soc. <u>85</u>, 2149-2154 (1963); J.L. Krstenansky, *et al.*, FEBS Lett. <u>211</u>, 10 (1987). Monoclonal antibodies binding to the protein of the invention may be useful diagnostic agents for the immunodetection of the protein. Neutralizing monoclonal antibodies binding to the protein may also be useful therapeutics for both conditions associated with the protein and also in the treatment of some forms of cancer where abnormal expression of the protein is involved. In the case of cancerous cells or leukemic cells, neutralizing monoclonal antibodies against the protein may be useful in detecting and preventing the metastatic spread of the cancerous cells, which may be mediated by the protein.

15

For compositions of the present invention which are useful for bone, cartilage, tendon or ligament regeneration, the therapeutic method includes administering the composition topically, systematically, or locally as an implant or device. When administered, the therapeutic composition for use in this invention is, of course, in a pyrogen-free, physiologically acceptable form. Further, the composition may desirably be encapsulated or injected in a viscous form for delivery to the site of bone, cartilage or tissue damage. Topical administration may be suitable for wound healing and tissue repair. Therapeutically useful agents other than a protein of the invention which may also optionally be included in the composition as described above, may alternatively or additionally, be administered simultaneously or sequentially with the composition in the methods of the invention. Preferably for bone and/or cartilage formation, the composition would include a matrix capable of delivering the protein-containing

5

15

20

composition to the site of bone and/or cartilage damage, providing a structure for the developing bone and cartilage and optimally capable of being resorbed into the body. Such matrices may be formed of materials presently in use for other implanted medical applications.

The choice of matrix material is based on biocompatibility, biodegradability, mechanical properties, cosmetic appearance and interface properties. The particular application of the compositions will define the appropriate formulation. Potential matrices for the compositions may be biodegradable and chemically defined calcium sulfate, tricalciumphosphate, hydroxyapatite, polylactic acid, polyglycolic acid and polyanhydrides. Other potential materials are biodegradable and biologically well-defined, such as bone or dermal collagen. Further matrices are comprised of pure proteins or extracellular matrix components. Other potential matrices are nonbiodegradable and chemically defined, such as sintered hydroxapatite, bioglass, aluminates, or other ceramics. Matrices may be comprised of combinations of any of the above mentioned types of material, such as polylactic acid and hydroxyapatite or collagen and tricalciumphosphate. The bioceramics may be altered in composition, such as in calcium-aluminate-phosphate and processing to alter pore size, particle size, particle shape, and biodegradability.

Presently preferred is a 50:50 (mole weight) copolymer of lactic acid and glycolic acid in the form of porous particles having diameters ranging from 150 to 800 microns. In some applications, it will be useful to utilize a sequestering agent, such as carboxymethyl cellulose or autologous blood clot, to prevent the protein compositions from disassociating from the matrix.

A preferred family of sequestering agents is cellulosic materials such as alkylcelluloses (including hydroxyalkylcelluloses), including methylcellulose, ethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropyl-methylcellulose, and carboxymethylcellulose, the most preferred being cationic salts of carboxymethylcellulose (CMC). Other preferred sequestering agents include hyaluronic acid, sodium alginate, poly(ethylene glycol), polyoxyethylene oxide, carboxyvinyl polymer and poly(vinyl alcohol). The amount of sequestering agent useful herein is 0.5-20 wt%, preferably 1-10 wt% based on total formulation weight, which represents the amount necessary to prevent desorbtion of the protein from the polymer matrix and to provide appropriate handling of the composition, yet not so much that the progenitor cells are prevented from infiltrating the matrix, thereby providing the protein

the opportunity to assist the osteogenic activity of the progenitor cells.

In further compositions, proteins of the invention may be combined with other agents beneficial to the treatment of the bone and/or cartilage defect, wound, or tissue in question. These agents include various growth factors such as epidermal growth factor (EGF), platelet derived growth factor (PDGF), transforming growth factors (TGF-and TGF-), and insulin-like growth factor (IGF).

The therapeutic compositions are also presently valuable for veterinary applications. Particularly domestic animals and thoroughbred horses, in addition to humans, are desired patients for such treatment with proteins of the present invention.

The dosage regimen of a protein-containing pharmaceutical composition to be used in tissue regeneration will be determined by the attending physician considering various factors which modify the action of the proteins, e.g., amount of tissue weight desired to be formed, the site of damage, the condition of the damaged tissue, the size of a wound, type of damaged tissue (e.g., bone), the patient's age, sex, and diet, the severity of any infection, time of administration and other clinical factors. The dosage may vary with the type of matrix used in the reconstitution and with inclusion of other proteins in the pharmaceutical composition. For example, the addition of other known growth factors, such as IGF I (insulin like growth factor I), to the final composition, may also effect the dosage. Progress can be monitored by periodic assessment of tissue/bone growth and/or repair, for example, X-rays, histomorphometric determinations and tetracycline labeling.

Polynucleotides of the present invention can also be used for gene therapy. Such polynucleotides can be introduced either *in vivo* or *ex vivo* into cells for expression in a mammalian subject. Polynucleotides of the invention may also be administered by other known methods for introduction of nucleic acid into a cell or organism (including, without limitation, in the form of viral vectors or naked DNA).

Cells may also be cultured *ex vivo* in the presence of proteins of the present invention in order to proliferate or to produce a desired effect on or activity in such cells. Treated cells can then be introduced *in vivo* for therapeutic purposes.

30

25

10

Patent and literature references cited herein are incorporated by reference as if fully set forth.

What is claimed is:

1. An isolated protein encoded by a polynucleotide selected from the group consisting of:

- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:1;
- (b) a polynucleotide comprising the nucleotide sequence of SEQID NO:1 from nucleotide 19 to nucleotide 561;
- (c) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AK296\_1i deposited under accession number ATCC 98026;
- (d) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AK296\_1i deposited under accession number ATCC 98026;
- (e) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:2;
- (f) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:2 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:2; and
- (g) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(f) above.
- 2. A composition comprising the protein of claim 1 and a pharmaceutically acceptable carrier.
- 3. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:2;
  - (b) the amino acid sequence of SEQ ID NO:2 from amino acid 3 to amino acid 181;
  - (c) fragments of the amino acid sequence of SEQ ID NO:2, each fragment comprising eight consecutive amino acids of SEQ ID NO:2; and
- (d) the amino acid sequence encoded by the cDNA insert of clone AK296\_1i deposited under accession number ATCC 98026; the protein being substantially free from other mammalian proteins.

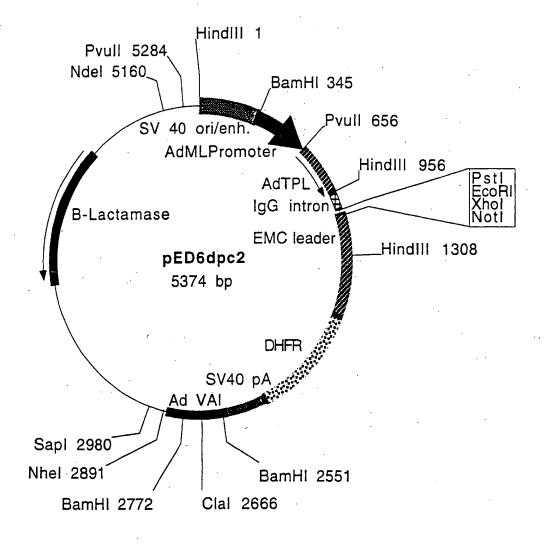
4. The protein of claim 3, wherein said protein comprises the amino acid sequence of SEQ ID NO:2.

- 5. The protein of claim 3, wherein said protein comprises a fragment of the amino acid sequence of SEQ ID NO:2, the fragment comprising eight consecutive amino acids of SEQ ID NO:2.
- 6. The protein of claim 3, wherein said protein comprises the amino acid sequence of SEQ ID NO:2 from amino acid 3 to amino acid 181.
- 7. A composition comprising the protein of claim 3 and a pharmaceutically acceptable carrier.
- 8. An isolated protein encoded by a polynucleotide selected from the group consisting of:
  - (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:21;
  - (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:21 from nucleotide 65 to nucleotide 490;
  - (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:21 from nucleotide 137 to nucleotide 490;
  - (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone AS34\_1i deposited under accession number ATCC 98026;
  - (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone AS34\_1i deposited under accession number ATCC 98026;
  - a polynucleotide comprising the nucleotide sequence of a mature protein coding sequence of clone AS34\_1i deposited under accession number ATCC 98026;
  - (g) a polynucleotide encoding a mature protein encoded by the cDNA insert of clone AS34\_1i deposited under accession number ATCC 98026;
  - (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:22;

(i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:22 having biological activity, the fragment comprising eight consecutive amino acids of SEQ ID NO:22; and

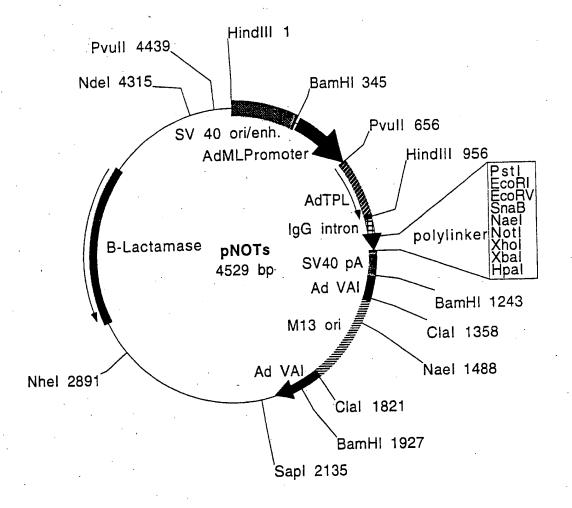
- (j) a polynucleotide which is an allelic variant of a polynucleotide of (a)-(g) above.
- 9. A protein comprising an amino acid sequence selected from the group consisting of:
  - (a) the amino acid sequence of SEQ ID NO:22;
  - (b) fragments of the amino acid sequence of SEQ ID NO:22, each fragment comprising eight consecutive amino acids of SEQ ID NO:22; and
- (c) the amino acid sequence encoded by the cDNA insert of clone AS34\_1i deposited under accession number ATCC 98026; the protein being substantially free from other mammalian proteins.

Fig. 1A



2/2

Fig. 1B



## SEQUENCE LISTING

```
<110> Jacobs, Kenneth
     McCoy, John M.
     LaVallie, Edward R.
     Collins-Racie, Lisa A.
     Evans, Cheryl
     Merberg, David
     Treacy, Maurice
     Bowman, Michael R.
     Genetics Institute, Inc.
<120> SECRETED PROTEINS
<130> GI 6505
<140>
<141>
<160> 154
<170> PatentIn Ver. 2.0
<210> 1
<211> 1248
<212> DNA
<213> Homo sapiens
<400> 1
aaaggcctac gtcgacctat gaccatgatt acgccaagct tggcacgagg cagggaggtc 60
ctgaccccaa cgagcacttc tgacaatgag accagagact cctcaattat tgatccagga 120
actgagcaag atcttccttc ccctgaaaat agttctgtta aagaataccg aatggaagtt 180
ccatcttcgt tttcagaaga catgtcaaat atcaggtcac agcatgcaga agaacagtcc 240
aacaatggta gatatgacga ttgtaaagaa tttaaagacc tccactgttc caaggattct 300
accotagoog aggaagaato tgagttooot totacttota tototgoagt totgtotgac 360
ttagetgact tgagaagetg tgatggccaa getttgccct cecaggacce tgaggttget 420
ttatetetea gttgtggcca ttecagagga etetttagte atatgcagca acatgacatt 480
ttagataccc tgtgtaggac cattgaatct acaatccatg tcgtcacaag gatatctggc 540
aaaggaaacc aagctgcttc ttgacattag gtgtagcatg tctactttta agtccctcac 600
ccccaaccc catgctgttt gtataagttt tgcttatttg tttttgtgct tcagtttgtc 660
cagtgetete tgettgaatg geaagataga tttatagget taattettgg teaggeagaa 720
ctccagatga aaaaaacttg catcttcagt atacttccta aaggycaatc agataatgga 780
tatgttttat gtaattaaga gttcacttta gtggctttca tttaatatgg ctgtctggga 840
agaacagggt tgcctagccc tgtacaatgt aatttaaact tacagcattt ttactgtgta 900
tgatatggtg teetetgtge cagttttgta cettatagag geagattgee teegateget 960
gtggttctta ttatcaaaat taagtttact tgtatacgga acaaccecaa gaaatttgat 1020
totgtaaaga atootottta gotgtggcot ggcagtatat aaatggtgot ttatttaaca 1080
gaatacctgt ggaggaaata aagcacactt gatgtaaaaa taattgtttt atttttattg 1140
acatgactga ttgattgcta ttctgtgcac ttaattaaac tgattgtgat gacttttaaa 1200
<210> 2
<211> 181
<212> PRT
<213> Homo sapiens
Met Thr Met Ile Thr Pro Ser Leu Ala Arg Gly Arg Glu Val Leu Thr
                 5
                                    10
```

Pro Thr Ser Thr Ser Asp Asn Glu Thr Arg Asp Ser Ser Ile Ile Asp 25 Pro Gly Thr Glu Gln Asp Leu Pro Ser Pro Glu Asn Ser Ser Val Lys 40 Glu Tyr Arg Met Glu Val Pro Ser Ser Phe Ser Glu Asp Met Ser Asn 55 Ile Arg Ser Gln His Ala Glu Glu Gln Ser Asn Asn Gly Arg Tyr Asp 70 Asp Cys Lys Glu Phe Lys Asp Leu His Cys Ser Lys Asp Ser Thr Leu Ala Glu Glu Glu Ser Glu Phe Pro Ser Thr Ser Ile Ser Ala Val Leu 100 105 Ser Asp Leu Ala Asp Leu Arg Ser Cys Asp Gly Gln Ala Leu Pro Ser 120 Gln Asp Pro Glu Val Ala Leu Ser Leu Ser Cys Gly His Ser Arg Gly 135 Leu Phe Ser His Met Gln Gln His Asp Ile Leu Asp Thr Leu Cys Arg 150 155 Thr Ile Glu Ser Thr Ile His Val Val Thr Arg Ile Ser Gly Lys Gly 165 170 Asn Gln Ala Ala Ser 180 <210> 3 <211> 1706 <212> DNA <213> Homo sapiens <400> 3

gcgcagtgaa gcagtgggaa ccggaatatc caaagagtgg tttgaaggag aaagaagcat 60 tgtggcttta tatcctctgg gcctgggttt cctgaagtca ccacacatag aggagagaa 120 aaatggctga gttaaagtac atttctggat ttgggaatga gtgttcttca gaggatcctc 180 getgeecagg tteectgeea gaaggacaga ataateetea ggtetgeece tacaatetet 240 atgctgagca gctctcagga tcggctttca cttgtccacg gagcaccaat aagagaagct 300 ggctgtatag gattctacct tcagtttctc acaagccctt tgaatccatt gacgaaggcc 360 atgtcactca caactgggat gaagttgatc ctgatcctaa ccagcttaga tggaaaccat 420 ttgagattcc aaaagcatct cagaagaaag tagactttgt gagtggcctg catacettgt 480 gtggagetgg agacataaag tetaacaatg ggettgetat ecacatttte etetgeaata 540 cctccatgga gaacagatgc ttttacaatt cagatgggga cttcttgatt gttccgcaga 600 aagggaacct teteatttac accgagtttg geaagatget tgtacagece aatgagatet 660 gcgtcattca gagaggaatg cggttcagca tagatgtctt tgaggagacc aggggctaca 720 tettggaggt ctatggtgte caetttgagt tacetgaeet tggaccaatt ggggecaatg 780 gcttggccaa tcctcgtgat ttcttgatac ccattgcctg gtatgaggat cgccaagtac 840 caggtggtta cacggtcatt aataaatacc agggcaagct gtttgctgcc aaacaggatg 900 teteceegtt caatgitgig geetggeacg ggaattatac accetacaag tacaacetga 960 agaatttcat ggttatcaac tcagtggcct ttgaccatgc agacccatcc attttcacag 1020 tattgactgc taaqtctqtc cqccctggag tggccattgc tgattttgtc atcttcccac 1080 ctcgatgggg ggttgctgat aagacettca ggceteetta ttaccatagg aactgcatga 1140 gtgagttcat gggactcatc cgaggtcact atgaggcaaa gcaaggtggg ttcctgccag 1200

ggggagggag tetacacage acaatgacee cecatggace tgatgetgae tgetttgaga 1260 aggccagcaa ggtcaagctg gcacctgaga ggattgccga tggcaccatg gcatttatgt 1320 ttgaatcatc tttaagtctg gcggtcacaa agtggggact caaggcctcc aggtgtttgg 1380 atgagaacta ccacaagtgc tgggagccac tcaagagcca cttcactccc aactccagga 1440 acceageaga acctaattga gaetggaaca ttgctaccat aattaagagt agatttgtga 1500 agatttette agaateteat getttetggt agtattggag gagggggttg gttaaaatga 1560 aaattcactt ttcatagtca agtaactcag aacttttatg gaaacgcatt tgcaaagttc 1620 aaaaaaaa aaaaaaaaa aaaaaa <210> 4 <211> 445 <212> PRT <213> Homo sapiens <400> 4 Met Ala Glu Leu Lys Tyr Ile Ser Gly Phe Gly Asn Glu Cys Ser Ser Glu Asp Pro Arg Cys Pro Gly Ser Leu Pro Glu Gly Gln Asn Asn Pro 25 Gln Val Cys Pro Tyr Asn Leu Tyr Ala Glu Gln Leu Ser Gly Ser Ala . 40 Phe Thr Cys Pro Arg Ser Thr Asn Lys Arg Ser Trp Leu Tyr Arg Ile Leu Pro Ser Val Ser His Lys Pro Phe Glu Ser Ile Asp Glu Gly His 70 Val Thr His Asn Trp Asp Glu Val Asp Pro Asp Pro Asn Gln Leu Arg 85 90 Trp Lys Pro Phe Glu Ile Pro Lys Ala Ser Gln Lys Lys Val Asp Phe Val Ser Gly Leu His Thr Leu Cys Gly Ala Gly Asp Ile Lys Ser Asn 120 Asn Gly Leu Ala Ile His Ile Phe Leu Cys Asn Thr Ser Met Glu Asn 135 Arg Cys Phe Tyr Asn Ser Asp Gly Asp Phe Leu Ile Val Pro Gln Lys Gly Asn Leu Leu Ile Tyr Thr Glu Phe Gly Lys Met Leu Val Gln Pro Asn Glu Ile Cys Val Ile Gln Arg Gly Met Arg Phe Ser Ile Asp Val 180 185

Glu Leu Pro Asp Leu Gly Pro Ile Gly Ala Asn Gly Leu Ala Asn Pro 210 215 220

Phe Glu Glu Thr Arg Gly Tyr Ile Leu Glu Val Tyr Gly Val His Phe 195 200 205

Arg Asp Phe Leu Ile Pro Ile Ala Trp Tyr Glu Asp Arg Gln Val Pro 225 230 235 240

Gly Gly Tyr Thr Val Ile Asn Lys Tyr Gln Gly Lys Leu Phe Ala Ala 245 250 Lys Gln Asp Val Ser Pro Phe Asn Val Val Ala Trp His Gly Asn Tyr 265 Thr Pro Tyr Lys Tyr Asn Leu Lys Asn Phe Met Val Ile Asn Ser Val 280 285 Ala Phe Asp His Ala Asp Pro Ser Ile Phe Thr Val Leu Thr Ala Lys 295 Ser Val Arg Pro Gly Val Ala Ile Ala Asp Phe Val Ile Phe Pro Pro 310 315 Arg Trp Gly Val Ala Asp Lys Thr Phe Arg Pro Pro Tyr Tyr His Arg 325 330 Asn Cys Met Ser Glu Phe Met Gly Leu Ile Arg Gly His Tyr Glu Ala Lys Gln Gly Gly Phe Leu Pro Gly Gly Gly Ser Leu His Ser Thr Met 355 360 Thr Pro His Gly Pro Asp Ala Asp Cys Phe Glu Lys Ala Ser Lys Val 375 380 . Lys Leu Ala Pro Glu Arg Ile Ala Asp Gly Thr Met Ala Phe Met Phe 395 Glu Ser Ser Leu Ser Leu Ala Val Thr Lys Trp Gly Leu Lys Ala Ser 405 Arg Cys Leu Asp Glu Asn Tyr His Lys Cys Trp Glu Pro Leu Lys Ser 420 425 His Phe Thr Pro Asn Ser Arg Asn Pro Ala Glu Pro Asn 440 <210> 5 <211> 912 <212> DNA <213> Homo sapiens <400> 5 gtggaaattt gtggctagtg tgatttttgt ttgtttcctt ttaagtactg ttgatcagtt 60 gtgacactta ctggttaaac ttacgttgct aaagatttct ctataataag ccacacatta 120 tatttagact atattaaggg accttggttt tcttctagat agcagctgtc ccaaagaaaa 180 tatttettet tigtetgita agaittaget attatetgee agitgitaag aggittiggi 240 tecaaaetea accageaatg ttgagagetg aaettaagat agetgttgta etttttgett 300 tecatetgtt actgteette attettgget cectactate tataaacage tgetgtgaag 360 aagaaaagtt gaataagagt tggcttaaat tttaaaaaaag aaaaagaaaa ttgaggtttt 420 aggattttca tggtaacaag ctctggtata agctaaggct ggcaagttca gatactaaaa 480 tattatttga tcatatcttg gatccttttg aaaaagttaa gactatatga aggtaaatta 540 gaaataagta tgaatattaa taaaatagCa tttatcttat ttctctattt tatgttgkga 600 mttaacctaa ttttatttt ttaamatttt yttatttytt ataatatgaa tgstgatatt 660

taaaggtaga tytatgtggt attytttgtg tityttaatt gittaamtyt taagattatt 720 tgtgatytgg atttatgtat tigttagata matacgratt gittaaaatgg ratgcaagit 780

```
tttcaaaagc ccaggtytaa atgtaatggk tggtttattg ttytataacc ccagcccatc 840
attitytgtg taaatyataa acaataaaca gratatamic ggtggtcatt tytaaaaaaa 900
aaaaaaaaa aa
<210> 6
<211> 45
<212> PRT
<213> Homo sapiens
<400> 6
Met Leu Arg Ala Glu Leu Lys Ile Ala Val Val Leu Phe Ala Phe His
                                     10
Leu Leu Ser Phe Ile Leu Gly Ser Leu Leu Ser Ile Asn Ser Cys
                                 25
Cys Glu Glu Glu Lys Leu Asn Lys Ser Trp Leu Lys Phe
                             40 .
<210> 7
<211> 1767
<212> DNA
<213> Homo sapiens
<400> 7
cgaagatgaa attecttate ttegeatttt teggtggtgt teacetttta teeetgtget 60
ctgggaaagc tatatgcaag aatggcatct ctaagaggac ttttgaagaa ataaaagaag 120
aaatagccag ctgtggagat gttgctaaag caatcatcaa cctagctgtt tatggtaaag 180
cccagaacag atcctatgag cgattggcac ttctggttga tactgttgga cccagactga 240
gtggctccaa gaacctagaa aaagccatcc aaattatgta ccaaaacctg cagcaagatg 300
ggctggagaa agttcacctg gagccagtga gaatacccca ctgggagagg ggagaagaat 360
cagctgtgat gctggagcca agaattcata agatagccat cctgggtctt ggcagcagca 420
ttgggactcc tccagaaggc attacagcag aagttctggt ggtgacctct ttcgatgaac 480
tgcagagaag ggcctcagaa gcaagaggga agattgttgt ttataaccaa ccttacatca 540
actactcaag gacggtgcaa taccgaacgc aggggggggt ggaagctgcc aaggtggggg 600
ctttggcatc totcattcga tccgtggcct ccttctccat ctacagtcct cacacaggta 660
ttcaggaata ccaggatggc gtgcccaaga ttccaacagc ctgtattacg gtggaagatg 720
cagaaatgat gtcaagaatg gcttctcatg ggatcaaaat tgtcattcag ctaaagatgg 780
gggcaaagac ctacccagat actgattcct tcaacactgt agcagagatc actgggagca 840
aatatccaga acaggttgta ctggtcagtg gacatctgga cagctgggat gttgggcagg 900
gtgccatgga tgatggcggt ggagccttta tatcatggga agcactctca cttattaaag 960
atcttgggct gcgtccaaag aggactctgc ggctggtgct ctggactgca ggagaacaag 1020
gtggagttgg tgccttccag tattatcagt tacacaaggt aaatatttcc aactacagtc 1080
tggtgatgga gtctgacgca ggaaccttct tacccactgg gctgcaattc actggcagtg 1140
aaaaggccag ggccatcatg gaggaggtta tgagcctgct gcagcccctc aatatcactc 1200
aggtcctgag ccatggagaa gggacagaca tcaacttttg gatccaagct ggagtgcctg 1260
gagccagtet acttgatgae ttatacaagt atttettett ceateactee caeggagaca 1320
ccatgactgt catggateca aagcagatga atgttgctgc tgctgtttgg gctgttgttt 1380
cttatgttgt tgcagacatg gaagaaatgc tgcctaggtc ctagaaacag taagaaagaa 1440
acgttttcat gettetggee aggaateetg ggtetgeaac tttggaaaac teetetteac 1500
ataacaattt catccaattc atcttcaaag cacaactcta tttcatgctt tctgttatta 1560
tettettga taettteeaa attetetgat tetagaaaaa ggaateatte teeeeteeet 1620
cccaccacat agaatcaaca tatggtaggg attacagtgg gggcatttct ttatatcacc 1680
tettaaaaac attgttteea etttaaaagt aaacaettaa taaatttttg gaagatetet 1740
gaaaaaaaa aaaaaaaa aaaaaaa
<210> 8
<211> 472
<212> PRT
```

<213> Homo sapiens

<400> 8

- Met Lys Phe Leu Ile Phe Ala Phe Phe Gly Gly Val His Leu Leu Ser 1 5 10 15
- Leu Cys Ser Gly Lys Ala Ile Cys Lys Asn Gly Ile Ser Lys Arg Thr
- Phe Glu Glu Ile Lys Glu Glu Ile Ala Ser Cys Gly Asp Val Ala Lys 35 40 45
- Ala Ile Ile Asn Leu Ala Val Tyr Gly Lys Ala Gln Asn Arg Ser Tyr 50 55 60
- Glu Arg Leu Ala Leu Leu Val Asp Thr Val Gly Pro Arg Leu Ser Gly 65 70 75 80
- Ser Lys Asn Leu Glu Lys Ala Ile Gln Ile Met Tyr Gln Asn Leu Gln 85 90 95
- Gln Asp Gly Leu Glu Lys Val His Leu Glu Pro Val Arg Ile Pro His 100 105 110
- Trp Glu Arg Gly Glu Glu Ser Ala Val Met Leu Glu Pro Arg Ile His 115 120 125
- Lys Ile Ala Ile Leu Gly Leu Gly Ser Ser Ile Gly Thr Pro Pro Glu 130 135 140 .
- Gly Ile Thr Ala Glu Val Leu Val Val Thr Ser Phe Asp Glu Leu Gln 145 150 155 160
- Arg Arg Ala Ser Glu Ala Arg Gly Lys Ile Val Val Tyr Asn Gln Pro 165 170 175
- Tyr Ile Asn Tyr Ser Arg Thr Val Gln Tyr Arg Thr Gln Gly Ala Val 180 185 190
- Glu Ala Ala Lys Val Gly Ala Leu Ala Ser Leu Ile Arg Ser Val Ala 195 200 205
- Ser Phe Ser Ile Tyr Ser Pro His Thr Gly Ile Gln Glu Tyr Gln Asp 210 215 220
- Gly Val Pro Lys Ile Pro Thr Ala Cys Ile Thr Val Glu Asp Ala Glu 225 230 235 240
- Met Met Ser Arg Met Ala Ser His Gly Ile Lys Ile Val Ile Gln Leu 245 250 255
- Lys Met Gly Ala Lys Thr Tyr Pro Asp Thr Asp Ser Phe Asn Thr Val 260 265 270
- Ala Glu Ile Thr Gly Ser Lys Tyr Pro Glu Gln Val Val Leu Val Ser 275. 280 285
- Gly His Leu Asp Ser Trp Asp Val Gly Gln Gly Ala Met Asp Asp Gly 290 295 300

Gly Gly Ala Phe Ile Ser Trp Glu Ala Leu Ser Leu Ile Lys Asp Leu 310 Gly Leu Arg Pro Lys Arg Thr Leu Arg Leu Val Leu Trp Thr Ala Gly 330 335 Glu Gln Gly Gly Val Gly Ala Phe Gln Tyr Tyr Gln Leu His Lys Val 345 Asn Ile Ser Asn Tyr Ser Leu Val Met Glu Ser Asp Ala Gly Thr Phe Leu Pro Thr Gly Leu Gln Phe Thr Gly Ser Glu Lys Ala Arg Ala Ile 375 Met Glu Glu Val Met Ser Leu Leu Gln Pro Leu Asn Ile Thr Gln Val Leu Ser His Gly Glu Gly Thr Asp Ile Asn Phe Trp Ile Gln Ala Gly 405 410 Val Pro Gly Ala Ser Leu Leu Asp Asp Leu Tyr Lys Tyr Phe Phe Phe 420 425 His His Ser His Gly Asp Thr Met Thr Val Met Asp Pro Lys Gln Met Asn Val Ala Ala Ala Val Trp Ala Val Val Ser Tyr Val Val Ala Asp 455 Met Glu Glu Met Leu Pro Arg Ser 465 470 <210> 9 <211> 571 <212> DNA <213> Homo sapiens <400> 9 cacgaggggt tttgacaagg cctatgttgt ccttggccag tttctggtgc taaagaaaga 60 tgaagacctc ttccgggaat ggctgaaaga cacttgtggc gccaacgcca agcagtcccg 120 ggactgcttc ggatgccttc gagagtggtg cgacgccttc ttgtgatgct ctctgggaag 180 ctctcaatcc ccagcctca tccagagttt gcagccgagt agggactcct cccctgtcct 240 ctacgaagga aaagattgct attgtcgtac tcacctccga cgtactccgg ggtcttttgg 300 gagttttete cectaaceat ticaactttt titiggattet egetetigea tgeeteecee 360 gtcctttttc ccttgccagt tccctggtga Cagttaccag ctttcctgaa tggattcccg 420 gccccatccc tcaccccac cctcactttc aatccgtttg ataccatttg gctcctttt 480 tggcagaaca gtcactgtcc ttgtaaagtt ttttagatca ataaagtcag tggctttcaa 540 ааааааааа аааааааааа аааааааааа а <210> 10 <211> 124 <212> PRT <213> Homo sapiens <400> 10 Lys Thr Leu Val Ala Pro Thr Pro Ser Ser Pro Gly Thr Ala Ser Asp 10

```
Ala Phe Glu Ser Gly Ala Thr Pro Ser Cys Asp Ala Leu Trp Glu Ala
                                 25
Leu Asn Pro Gln Pro Ser Ser Arg Val Cys Ser Arg Val Gly Thr Pro
                             40
Pro Leu Ser Ser Thr Lys Glu Lys Ile Ala Ile Val Val Leu Thr Ser
                         55
Asp Val Leu Arg Gly Leu Leu Gly Val Phe Ser Pro Asn His Phe Asn
 65
                     70
Phe Phe Trp Ile Leu Ala Leu Ala Cys Leu Pro Arg Pro Phe Ser Leu
Ala Ser Ser Leu Val Thr Val Thr Ser Phe Pro Glu Trp Ile Pro Gly
            100
                                105
                                                    110
Pro Ile Pro His Pro His Pro His Phe Gln Ser Val
                            120
<210> 11
<211> 1713
<212> DNA
<213> Homo sapiens
<400> 11
gggcaggata ttagaaatgg ctactcccca gtcaattttc atctttgcaa tctgcatttt 60
aatgataaca gaattaattc tggcctcaaa aagctactat gatatcttag gtgtgccaaa 120
ateggeatea gagegeeaaa teaagaagge ettteacaag ttggeeatga agtaecaece 180
tgacaaaaat aagagcccag atgctgaagc aaaattcaga gagattgcag aagcatatga 240
aacactctca gatgctaata gacgaaaaga gtatgataca cttggacaca gtgcttttac 300
tagtggtaaa ggacaaagag gtagtggaag ttcttttyag cagtcattta acttcaattt 360-
tgatgactta tttaaagact ttggcttttt tggtcaaaac caaaacactg gatccaagaa 420
gcgttttgaa aatcatttcc agacacgcca ggatggtggt tccagtagac aaaggcatca 480
tttccaagaa ttttcttttg gaggtggatt atttgatgac atgtttgaag atatggagaa 540
aatgttttct tttagtggtt ttgactctac caatcagcat acagtacaga ctgaaaatag 600
atttcatgga tctagcaagc actgcaggac tgtcactcaa cgaagaggaa atatggttac 660
tacatacact gactgttcag gacagtagtt cttattctat tctcactaaa tccaactggt 720
tgactottcc tcattatctt tgatgctaaa caattttctg tgaactattt tgacaagtgc 780
atgatttcac tttaaacaat ttgatatagc tattaaatat atttaagggt ttttttttt 840
gacaaattca acattcaacg agtagacaaa atgctaatta tttccctgat taggaaagtt 900
tetttaaaaa acaegtaatt ttgeetagtg etttttetet acetgeeett gggeteacta 960
atatcaccag tattattacc aagaaaatat tgagtttacc tgattaaact ttaaaagtta 1020
attgtagatt taaattgtgt gaacctaatg atttttgcag tgaaaccttt actaattcaa 1080
agttgcatgt tctatgacat ctgtgacttg cgttgcagag tgtacatgaa actgtataat 1140
tgagtcattc agtaaaggag aacagtatct tggttaattg ctactgaaag gttgagaaag 1200
gaatggtttg atatttacca cagcgctgtg cctttctaca gtagaactgg ggtaaaggaa 1260
atggttttat tgcccatagt catttaggct ggaaaaaagt tgaaaactta acgaaatatt 1320
gccaagagat tgttatgtgt ttggttccag cctaaaaatg attttgtagt gttgaaatca 1380
tagctactta catagettit teatattiet tiettaging tiggeactet taggiettag 1440
tatggattta tgtgtttgtg tgtgtgtagt ttatcctctc tctcatcttt atctagagat 1500
tgactgatac ctcattctgt ttgtaaaacc agccagtaat ttctgtgcaa ccttactatg 1560
tgcaatattt ttaaatcctg agaaatgtgt gcttttgttt tcggatagac ttatttcttt 1620
agttotgoac tittocacat tatactocat atgagtatta atoctatgga tacatattaa 1680
aacaagtgtc tcataaaaaa aaaaaaaaaa aaa
                                                                  1713
<210> 12
```

8

<211> 223

<212> PRT

<213> Homo sapiens

<400> 12

Met Ala Thr Pro Gln Ser Ile Phe Ile Phe Ala Ile Cys Ile Leu Met
1 5 10 15

Ile Thr Glu Leu Ile Leu Ala Ser Lys Ser Tyr Tyr Asp Ile Leu Gly
20 25 30

Val Pro Lys Ser Ala Ser Glu Arg Gln Ile Lys Lys Ala Phe His Lys 35 40 45

Leu Ala Met Lys Tyr His Pro Asp Lys Asn Lys Ser Pro Asp Ala Glu 50 60 .

Ala Lys Phe Arg Glu Ile Ala Glu Ala Tyr Glu Thr Leu Ser Asp Ala 65 70 75 80

Asn Arg Arg Lys Glu Tyr Asp Thr Leu Gly His Ser Ala Phe Thr Ser 85 90 95

Gly Lys Gly Gln Arg Gly Ser Gly Ser Ser Phe Glu Gln Ser Phe Asn 100 105 110

Phe Asn Phe Asp Asp Leu Phe Lys Asp Phe Gly Phe Phe Gly Gln Asn 115 120 125

Gln Asn Thr Gly Ser Lys Lys Arg Phe Glu Asn His Phe Gln Thr Arg 130 135 140

Gln Asp Gly Gly Ser Ser Arg Gln Arg His His Phe Gln Glu Phe Ser 145 150 155 160

Phe Gly Gly Gly Leu Phe Asp Asp Met Phe Glu Asp Met Glu Lys Met 165. 170 175

Phe Ser Phe Ser Gly Phe Asp Ser Thr Asn Gln His Thr Val Gln Thr 180 185 190

Glu Asn Arg Phe His Gly Ser Ser Lys His Cys Arg Thr Val Thr Gln 195 200 205

Arg Arg Gly Asn Met Val Thr Thr Tyr Thr Asp Cys Ser Gly Gln 210 215 220

<210> 13

<211> 505

<212> DNA

<213> Homo sapiens

<220>

<221> unsure '

<222> (430)

<220>

<221> unsure

<222> (436)

```
<220>
<221> unsure
<222> (452)
<400> 13
gaattcggca cgagggcgcg gggtccgywa tggcgscggc agccgaaggc gtactggcga 60
cccggagtga tgagcccgcc cgagacgatg ccsccgtgga gacagctgag gaarcaaagg 120
agcctgctga aagctgacat cactgagctc tgccgggaca tgttctccaa aatggccact 180
tacctgactg gggaactgac ggccaccagt gaagactata agctcctgga aaatatgaat 240
aaactcacca gcttgaagta tyttgaaatg aaagatattg ctataaacat tagtaggaac 300
ttaaaaggact taaaccagaa atatgctgga ctgcagcctt atytggattc agattcaatg 360
ttcattggaa gagcaggtag cagctttttg agcaggcagc ttacaagttg grtgcmtwtt 420
tcaaaaaaan tggaanccca agtacaagaa gntggagaag cgatgagaaa attatttta 480
tgggacagag ttttttttt ttaat
<210> 14
<211> 144
<212> PRT
<213> Homo sapiens
<220>
<221> UNSURE
<222> (65)
<220>
<221> UNSURE
<222> (115)..(117)
<220>
<221> UNSURE
<222> (121)
<220>
<221> UNSURE
<222> (123)
<220>
<221> UNSURE
<222> (128)
<400> 14
Met Ser Pro Pro Glu Thr Met Pro Pro Trp Arg Gln Leu Arg Lys Gln
                                     10
Arg Ser Leu Leu Lys Ala Asp Ile Thr Glu Leu Cys Arg Asp Met Phe
                                 25
Ser Lys Met Ala Thr Tyr Leu Thr Gly Glu Leu Thr Ala Thr Ser Glu
                             40
Asp Tyr Lys Leu Leu Glu Asn Met Asn Lys Leu Thr Ser Leu Lys Tyr
     50
Xaa Glu Met Lys Asp Ile Ala Ile Asn Ile Ser Arg Asn Leu Lys Asp
                                         75
Leu Asn Gln Lys Tyr Ala Gly Leu Gln Pro Tyr Leu Asp Ser Asp Ser
                                     90
Met Phe Ile Gly Arg Ala Gly Ser Ser Phe Leu Ser Arg Gln Leu Thr
```

100 105 110 Ser Trp Xaa Xaa Xaa Ser Lys Lys Xaa Glu Xaa Gln Val Gln Glu Xaa Gly Glu Ala Met Arg Lys Leu Phe Leu Trp Asp Arg Val Phe Phe Phe 135 <210> 15 <211> 315 <212> DNA <213> Homo sapiens <220> <221> unsure <222> (65) <220> <221> unsure <222> (163) <220> <221> unsure <222> (269) <220> <221> unsure <222> (275) <400> 15 gcagcttatc accttgtyaa tgtcggtaac ttacttttcc ataatattgc aaataacata 60 aaatnttaaa ataatteeaa getgagtttt etagattgag cagaaatggt gaaaggagta 120 ttgataactt ggcgtatgtg atgggcccct cttgtttatt ttntatgtga gtcacattga 180 catgcgatca gtttggggaa atgtgatgaa aacaaagact agatgggtat gtgtgtttat 240 gtgttgggta gggaggtgac gattgccant catanaataa aggattttat aaaataccaa 300 aaaaaaaaa aaaaa <210> 16 <211> 1719 <212> DNA <213> Homo sapiens <400> 16 aatttcacag ttacagtgca gaagcagaag caaaagaatt aaccagctct tcagtcaagc 60 aaatoctota otcaccatgo ttootootgo cattoattto tatotootto coottgoatg 120 catectaatg aaaagetgtt tggettttaa aaatgatgee acagaaatee tttatteaca 180 tgtggttaaa cctgttccag cacaccccag cagcaacagc acgttgaatc aagccagaaa 240 tggaggcagg catttcagta acactggact ggatcggaac actcgggttc aagtgggttg 300 ccgggaactg cgttccacca aatacatctc tgatggccag tgcaccagca tcagccctct 360 gaaggagctg gtgtgtgctg gcgagtgctt gcccctgcca gtgctcccta actggattgg 420 aggaggctat ggaacaaagt actggagcag gaggagctcc caggagtggc ggtgtgtcaa 480 tgacaaaacc cgtacccaga gaatccagct gcagtgccaa gatggcagca cacgcaccta 540

caaaatcaca gtagtcactg cctgcaagtg caagaggtac acccggcagc acaacgagtc 600 cagtcacaac tttgagagca tgtcacctgc caagccagtc cagcatcaca gagagcggaa 660 aagagccagc aaatccagca agcacagcat gagttagaac tcagactccc ataactagac 720 ttactagtaa ccatctgctt tacagatttg attgcttgga agactcaagc ctgccactgc 780 tgttttctca cttgaaagta tatgctttct gctttgatca aacccagcaa gctgtcttaa 840 gtatcaggac cttctttggg aatagttttt ccttttcaaga tttttcaaga tgtaggtata 900 tocatgaatg caatttgcat ttaaattcca cgtatcctgt agttttaatt cctcattgtt 960

cttaaaagac tgttgatact ataaacatca gtgaatcatt atattttaaa acagaaaagg 1020 getteteaga taccetecat etactggeec atcecetete etaaacaaaa eteetteaaa 1080 acaggttaaa aaaaatatgt tgtcatgaat cttcacagta acatttcaga aaggtgcttt 1140 tttggtactc ttcatgggaa cagtttagca gccatgagtg atcttccttt gaaagagaat 1200 gaaagaccct gtgacatttc acttcaaaaa taagccctgt agctctttac ggtcgcatag 1260 tatgaaatta taccctgcat gctgaccctc gcttggaatg gaatgccaga aatgcatggc 1320 agcagctaat aagtaaagct gattaactat ttatttgtca atgttattat ttaatgagct 1380 ttcacatgtg atttgtttca aaactttaat tttttaatgt tttgaaactt tttcatggac 1440 ctaaatattt tcctatatga tttgtggttg attagaaata tgaaatacat gttgtagata 1500 tgtaaaatga atattttagt ctccttatta catatatgtt catggtgaac tttatcaata 1560 gtatggatct ttttaaatca ataagatgct ttgtaaagtt gaaataagta atactttctt 1620 gtttaatctg tgcaatcaga aggtgtcttg accttcaatt caattggttt cttttaacaa 1680 aaataaacac tgctaaaagt taaaaaaaaa aaaaaaaaa <210> 17 <211> · 206 <212> PRT <213> Homo sapiens <400> 17 Met Leu Pro Pro Ala Ile His Phe Tyr Leu Leu Pro Leu Ála Cys Ile Leu Met Lys Ser Cys Leu Ala Phe Lys Asn Asp Ala Thr Glu Ile Leu Tyr Ser His Val Val Lys Pro Val Pro Ala His Fro Ser Ser Asn Ser Thr Leu Asn Gln Ala Arg Asn Gly Gly Arg His Phe Ser Asn Thr Gly Leu Asp Arg Asn Thr Arg Val Gln Val Gly Cys Arg Glu Leu Arg Ser 65 70 Thr Lys Tyr Ile Ser Asp Gly Gln Cys Thr Ser Ile Ser Pro Leu Lys 90 Glu Leu Val Cys Ala Gly Glu Cys Leu Pro Leu Pro Val Leu Pro Asn 105 Trp Ile Gly Gly Tyr Gly Thr Lys Tyr Trp Ser Arg Arg Ser Ser 120 Gln Glu Trp Arg Cys Val Asn Asp Lys Thr Arg Thr Gln Arg Ile Gln Leu Gln Cys Gln Asp Gly Ser Thr Arg Thr Tyr Lys Ile Thr Val Val 155 Thr Ala Cys Lys Cys Lys Arg Tyr Thr Arg Gln His Asn Glu Ser Ser 170 His Asn Phe Glu Ser Met Ser Pro Ala Lys Pro Val Gln His His Arg

Glu Arg Lys Arg Ala Ser Lys Ser Ser Lys His Ser Met Ser

200

195

```
<210> 18
      <211> 676
      <212> DNA
      <213> Homo sapiens
      <220>
      <221> unsure
      <222> (35)
      <220>
      <221> unsure
      <222> (151)
      <220>
      <221> unsure
      <222> (165)
      <220>
      <221> unsure
      <222> (229)
      <22Q>
      <221> unsure
      <222> (245)
      <220>
      <221> unsure
      <222> (612)
      <220>
      <221> unsure
      <222> (625)
<400> 18
      gagattttca gcacctgcg atatgcaagc cgagntcagc gggtcaccac ccgaccacag 60
      gcccccaagt ttcctgtggc aaagcagccc cagcgtttgg agacagagat gctgcagetc 120
      caggaggaga accgtcgcct gcagttccag ntggaccaaa tggantgcaa ggcctcaggg 180
      ttcagtggag cccgggtggc ctgggcccag cggaacctgt acgggatgnt acaggagttt 240
      catgntagag aatgagaggc tcaggaaaga aaagagccag ctgcagaata gccgagagct 300
      agcccagaat gagcagcgca tcctggccca gcaggtccat gcactagaga rgcgtctcct 360
      ctctgcctgc taccatcacc agcagggtcc tggcctgacc ccaccgtgtc cctgcttgat 420
      ggccccaget ecceettgee atgeaetgee acceetctae teetgeeeet getgeeaeat 480
      ctgcccactg tgtckagtgc ccctggccca ctgggyykgc ctgscmaggg gagcaccacc 540
      ttgccccagc ctctcttctg gggctctgar gagtcagaaa tagaccagac gtggtttcct 600
      ggttctcagg anggttttta gtttnaggag agggacggta gaagaaccat tttgttgcaa 660
      aaagaagggg accaag
                                                                         676
      <210> 19
      <211> 218
      <212> PRT
      <213> Homo sapiens
      <220>
      <221> UNSURE
      <222> (5)
      <220>
      <221> UNSURE
```

<222> (43)

```
<220>
<221> UNSURE
<222> (48)
<220>
<221> UNSURE
<222> (69)
<220>
<221> UNSURE
<222> (75)
<220>
<221> UNSURE
<222> (110)
<220>
<221> UNSURE
<222> (158)
<220>
<221> UNSURE
<222> (165)..(166)
<220>
<221> UNSURE
<222> (168)
<220>
<221> UNSURE
<222> (183)
<220>
<221> UNSURE
<222> (187)
<220>
<221> UNSURE
<222> (197)
<220>
<221> UNSURE
<222> (201)
<400> 19
Met Gln Ala Glu Xaa Ser Gly Ser Pro Pro Asp His Arg Pro Pro Ser
      5 10
Phe Leu Trp Gln Ser Ser Pro Ser Val Trp Arg Gln Arg Cys Cys Ser
                               25
Ser Arg Arg Arg Thr Val Ala Cys Ser Ser Xaa Trp Thr Lys Trp Xaa
                          40
Ala Arg Pro Gln Gly Ser Val Glu Pro Gly Trp Pro Gly Pro Ser Gly .
                       55
Thr Cys Thr Gly Xaa Tyr Arg Ser Phe Met Xaa Glu Asn Glu Arg Leu
65
                   70
                                       75
```

Arg Lys Glu Lys Ser Gln Leu Gln Asn Ser Arg Glu Leu Ala Gln Asn 85 90 95

Glu Gln Arg Ile Leu Ala Gln Gln Val His Ala Leu Glu Xaa Arg Leu 100 105 110

Leu Ser Ala Cys Tyr His His Gln Gln Gly Pro Gly Leu Thr Pro Pro 115 120 125

Cys Pro Cys Leu Met Ala Pro Ala Pro Pro Cys His Ala Leu Pro Pro 130 135 140

Leu Tyr Ser Cys Pro Cys Cys His Ile Cys Pro Leu Cys Xaa Val Pro 145 150 155 160

Leu Ala His Trp Xaa Xaa Leu Xaa Arg Gly Ala Pro Pro Cys Pro Ser 165 170 175

Leu Ser Ser Gly Ala Leu Xaa Ser Gln Lys Xaa Thr Arg Arg Gly Phe 180 185 190

Leu Val Leu Arg Xaa Val Phe Ser Xaa Arg Arg Gly Thr Val Glu Glu
195 200 205

Pro Phe Cys Cys Lys Lys Lys Gly Thr Lys 210 215

<210> 20

<211> 373

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (50)

<220×

<221> unsure

<222> (54)

<220>

<221> unsure

<222> (60)

<220>

<221> unsure

<222> (102)

<220>

<221> unsure

<222> (114)

<220>

<221> unsure

<222> (118)

<220>

<221> unsure

<222> (144)..(145)

```
<220>
<221> unsure
<222> (147)..(148)
<220>
<221> unsure
<222> (228)
<400> 20
ttccaaactt ggcccagaga ctggaggcct tcagagacca gattggcagn tccntgcgan 60
gtggccgcag ccagccaccc tgcagtgagg gcgcacggag cncaggccaa gtcntccntc 120
cccattgaag gccaagtggg aacnnannag aatgctgtgt gacctcagac tgggctccac 180
actittgggc ttcagtotgc coatotgctg aatggagaca gcagctgnta ctccacctqc 240
agctgggcta ggggcgggga ctgggggtgc tatttagggg aacaagggga tttcaggaga 300
aacccaggca gcaggggatg aaatacatga ataaagagag gcatcagctc caaaaaaaaa 360
aaaaaaaaa aaa
<210> 21
<211> 1485
<212> DNA
<213> Homo sapiens
<400> 21
ccccgcgttc tctaaactaa ctatttaaag gtctgcggtc gcaaatggtt tgactaaacg 60
taggatggga cttaagttga acggcagata tatttcactg atcctcgcgg tgcaaatagc 120
gtatctggtg caggccgtga gagcagcygg caagtgcgat gcggtcttca agggcttttc 180
ggactgtttg ctcaagctgg gcgacagcat ggccaactac ccgcagggcc tggacgacaa 240
gacgaacatc aagaccgtgt gcacatactg ggaggatttc cacagctgca cggtcacagc 300
ccttacggat tgccaggaag gggcgaaaga tatgtgggat aaactgagaa aagaatccaa 360
apaceteaac atecaaggea gettattega actetgegge ageggeaacg gggeggeggg 420
gtccctgctc ccggcgttcc cggtgctcct ggtgtctctc tcggcagctt tagcgacctg 480
gettteette tgagegtggg geeageteee eeegegegee caeceacaet caetecatge 540
tcccggaaat cgagaggaag atccattagt tctttgggga cgttgtgatt ctctgtgatg 600
ctgaaaacac tcatatagga ttgtgggaaa tcctgattct cttttttatt tcgtttgatt 660
tcttgtgttt tatttgccaa atgttaccaa tcagtgagca agcaagcaca gccaaaatcg 720
gacctcaget tragtccgtc treacacaca aaraagaaaa eggcaaaccc accccatttt 780
ttaattttat tattattaat tttttttgtt ggcaaaagaa tctcaggaac ggccctgggc 840
cacctactat attaatcatg ctagtaacat gaaaaatgat gggctcctcc taataggaag 900
gcgaggagag gagaaggcca ggggaatgaa ttcaagagag atgtccacgg acgaaacata 960
eggtgaataa tteaegetea egtegttett eeacagtate ttgttttgat cattteeact 1020
gcacatttct cctcaagaaa agcgaaagga cagactgttg gctttgtgtt tggaggatag 1080
gagggagaga gggaaggggc tgaggaaatc tctggggtaa gagtaaaggc ttccagaaga 1140
catgctgcta tggtcactga ggggttagct ttatctgctg ttgttgatgc atccgtccaa 1200
gttcactgcc tttattttcc ctcctcctc ttgttttagc tgttacacac acagtaatac 1260
ctgaatatcc aacggtatag atcacaaggg ggggatgtta aatgttaatc taaaatatag 1320
ctaaaaaaag attttgacat aaaagagcct tgattttaaa aaaaaaagag agagagatgt 1380
aatttaaaaa gtttattata aattaaattc agcaaaaaaa gatttgctac aaagtataga 1440
<210> 22
<211> 142
<212> PRT
<213> Homo sapiens
<400> 22
Met Gly Leu Lys Leu Asn Gly Arg Tyr Ile Ser Leu Ile Leu Ala Val
                                    10
Gln Ile Ala Tyr Leu Val Gln Ala Val Arg Ala Ala Gly Lys Cys Asp
```

20 25 30

Ala Val Phe Lys Gly Phe Ser Asp Cys Leu Leu Lys Leu Gly Asp Ser 35 40 45

Met Ala Asn Tyr Pro Gln Gly Leu Asp Asp Lys Thr Asn Ile Lys Thr 50 55 60

Val Cys Thr Tyr Trp Glu Asp Phe His Ser Cys Thr Val Thr Ala Leu 65 70 75 80

Thr Asp Cys Gln Glu Gly Ala Lys Asp Met Trp Asp Lys Leu Arg Lys 85 90 95

Glu Ser Lys Asn Leu Asn Ile Gln Gly Ser Leu Phe Glu Leu Cys Gly
100 105 110

Ser Gly Asn Gly Ala Ala Gly Ser Leu Leu Pro Ala Phe Pro Val Leu 115 120 125

Leu Val Ser Leu Ser Ala Ala Leu Ala Thr Trp Leu Ser Phe 130 135 140

<210> 23

<211> 825

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (290)

<220>

<221> unsure

<222> (480)

<220>

<221> unsure

<222> (491)

<220>

<221> unsure

<222> (589)

<220>

<221> unsure

<222> (698)

<400> 23

gaatteggca egagttttt tittetgeag tigtgitat giggittigt gigaagaaaa 60 acagactegg tecaggitaga aatggigagg agggggaaga gaattacatt tecaggitca 120 gaaactiggca aacagittic etakagigac tecagacaca cacagitaaca actologiciga 180 caattitatt titaattigag aaataaagat titeeteeag cacactigagg actologica 240 ccaccacaaa agcaagacet gitattataa geegaggitig caggigagetii aactigegiga 300 ccegiteaggg ceeegiggaa tecitegeag geegaggitig caggigagetii aactigegiga 360 teagitigiigi titegaggiga agcaagacet gigaaattii 480 tigeecagga iidaagaaga cittigaaaa titettaaaaa teagaatii aatacaagta 600

```
gttgtttaca tttcttgaaa aaataggaac tcgggcagca gaatcagatt ggcagaatct 660
ttagactaca caggcaataa tcaagtctgc tgttttgncc tttcgtagta gaagtggttg 720
tagtgtttag atatetgttt ggtettgett ettgtattge atttttttea ataaacaaca 780
acaaaaagaa aaaaaaaaa aaaaaaaaaa aagatcttta attaa
<210> 24
<211> 200
<212> PRT
<213> Homo sapiens
<220>
<221> UNSURE
<222> (75)
<220>
<221> UNSURE
<222> (86)
<220>
<221> UNSURE
<222> (89)
<220>
<221> UNSURE
<222> (118)
<220>
<221> UNSURE
<222> (122)
<220>
<221> UNSURE
<222> (134)
<220>
<221> UNSURE
<222> (152)
<220>
<221> UNSURE
<222> (158)
<220>
<221> UNSURE
<222> (199)
<400> 24
Met Arg Thr Leu Ala Pro Thr His Lys Ala Arg Pro Val Phe Ile Ser
                                     10
Arg Gly Cys Arg Glu Leu Asn Cys Gly Thr Arg Gln Gly Pro Val Asp
            20
                                 25
Pro Ser Pro Ser Pro Pro Pro Pro Pro Pro Leu Gly Pro Ile Ser Val
         35
Cys Trp Gly Gly Cys Leu Gly Ser Trp Gly Val Arg Glu Thr Thr Asn
     50
                         55
Leu Gly Glu Leu Gly Ala Arg Ala Ala Ala Xaa Leu Thr Pro Phe Asp
```

75 65 70 80 Ala His Gly Lys Phe Xaa Pro Arg Xaa Ser Ala Pro Gly Trp Leu Phe 85 90 Leu Gln Ile Ser Leu Lys Cys Ile Ile Leu Val Thr Lys Met Lys Glu 105 Leu Cys Lys Phe Phe Xaa Asn Tyr Glu Xaa Ile Ser Ser Ser Cys Leu 120 His Phe Leu Lys Lys Xaa Glu Leu Gly Gln Gln Asn Gln Ile Gly Arg Ile Phe Arg Leu His Arg Gln Xaa Ser Ser Leu Leu Phe Xaa Pro Phe 150 155 Val Val Glu Val Val Val Val Phe Arg Tyr Leu Phe Gly Leu Ala Ser 170 Cys Ile Ala Phe Phe Ser Ile Asn Asn Asn Lys Lys Lys Lys Lys 185 190 -180 Lys Lys Lys Asp Leu Xaa Leu 195 200 <210> 25 <211> 1096 <212> DNA <213> Homo sapiens <400> 25 tggctgcctt gacccagtgg caacactagc tgcagttatg acagagaagt ctccttttac 60 cacaccaatt ggtcgaaaag atgaagcaga tcttgcaaaa tcagctttgg ccatggcgga 120 ttcagaccac ctgacgatet acaatgcata tctaggatgg aagaaagcac gacaagaagg 180 aggitategi tetgaaatea catactgeeg gaggaactit ettaatagaa cateactgit 240 aaccctagag gatgtaaagc aggagttaat aaagttggtt aaggcagcag gattttcatc 300 ttccacaact tctaccaget gggaaggaaa cagageetea cagaeeetet cattecaaga 360 aattgeeett ettaaagetg taetggtgge tggactgtat gacaatgtgg ggaarataat 420 ctatacaaag tcagtggatg ttacagaaaa attggcttgc attgtggaga cggcccaagg 480 caaarcacaa gtacacccat cctcagtaaa tcgagatttg caaactcatg gatggctctt 540 ataccaggag aagataaggt atgccagagt gtatttgaga gaaactaccc taataacccc 600 ttttccattt ttactttttg gtggtgatat agaagttcag caccgagaac gtcttctttc 660 tattgatggc tggatctatt ttcaggcccc tgtaaagata gctgtcattt tcaagcagct 720 gagagttete attgatteag tittaagaaa aaagettgaa aateeaaaga tgteeettga 780 aaatgacaag attctgcaga tcattacgga attgataaaa acagagaata actgaaactg 840 aaattcatgg tcaactgctt taaaaattaa gatgaagata cagtcatgaa attatctgaa 900 aatgggtcat cacattaagt atttcattac ttaaaatgtt ggtactagcc attaacttaa 960 aggtggtggg aaaaaagcac atactttaaa catgtataat tttctagttt cctttttaat 1020 gatgattatt ctgaatgtat ttgccactac atttacaata aatttctttg gtattatgca 1080 1096 aaaaaaaaa aaaaaa <210> 26 <211> 265 <212> PRT <213> Homo sapiens <220> <221> UNSURE

<222> (150)

<400> 26

Met Thr Glu Lys Ser Pro Phe Thr Thr Pro Ile Gly Arg Lys Asp Glu 1 5 10 . 15

Ala Asp Leu Ala Lys Ser Ala Leu Ala Met Ala Asp Ser Asp His Leu 20 25 30

Thr Ile Tyr Asn Ala Tyr Leu Gly Trp Lys Lys Ala Arg Gln Glu Gly 35 40 45

Gly Tyr Arg Ser Glu Ile Thr Tyr Cys Arg Arg Asn Phe Leu Asn Arg 50 55 60

Thr Ser Leu Leu Thr Leu Glu Asp Val Lys Gln Glu Leu Ile Lys Leu 65 70 75 80

Val Lys Ala Ala Gly Phe Ser Ser Ser Thr Thr Ser Thr Ser Trp Glu 85 90 95

Gly Asn Arg Ala Ser Gln Thr Leu Ser Phe Gln Glu Ile Ala Leu Leu 100 105 110

Lys Ala Val Leu Val Ala Gly Leu Tyr Asp Asn Val Gly Lys Ile Ile
115 120 125

Tyr Thr Lys Ser Val Asp Val Thr Glu Lys Leu Ala Cys Ile Val Glu 130 135 140

Thr Ala Gln Gly Lys Xaa Gln Val His Pro Ser Ser Val Asn Arg Asp 145 150 155 160

Leu Gln Thr His Gly Trp Leu Leu Tyr Gln Glu Lys Ile Arg Tyr Ala 165 170 175

Arg Val Tyr Leu Arg Glu Thr Thr Leu Ile Thr Pro Phe Pro Phe Leu 180 185 190

Leu Phe Gly Gly Asp Ile Glu Val Gln His Arg Glu Arg Leu Leu Ser 195 200 205

Ile Asp Gly Trp Ile Tyr Phe Gln Ala Pro Val Lys Ile Ala Val Ile 210 215 220

Phe Lys Gln Leu Arg Val Leu Ile Asp Ser Val Leu Arg Lys Lys Leu 225 230 235 240

Glu Asn Pro Lys Met Ser Leu Glu Asn Asp Lys Ile Leu Gln Ile Ile 245 250 255

Thr Glu Leu Ile Lys Thr Glu Asn Asn 260 265

<210> 27

<211> 423

<212> DNA

<213> Homo sapiens

```
<220>
 <221> unsure
 <222> (13)..(14)
 <220>
 <221> unsure
 <222> (18)
 <220>
 <221> unsure
 <222> (412)
<400> 27
 gaattcggca cgnngtgnaa tataaaaatt tatttttaag tcaaagtatg caacaaataa 60
 acctacagaa aacattttcc catcacaatc tgttgcttta ccaaataata ttttgaaaac 120
 acattccttc agtcattata aagttcttaa aatacaaaag aaattaaatc tgtaagaaag 180
 totagtagac cagatgctgt tgtcaagact tgtatgttgg tgtttttgct ttcagtacat 240
 cccacgccat ccacctccac tycatgccgc cttgcccata gtaacctcca ctgcctccac 300
 caccacggcc ataaccaccc aaaccatcag gagtaccata tcctccactg taattgttcc 360
 ccattcccat tettecaact ggattccata ggccytecet ggattatttt tnaaaaggaa 420
 aaa
 <210> 28
 <211> 76
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> UNSURE
 <222> (66)
 <220>
 <221> UNSURE
 <222> (68)
 <220>
 <221> UNSURE
 <222> (73)
 <400> 28
 Met Leu Leu Ser Arg Leu Val Cys Trp Cys Phe Cys Phe Gln Tyr Ile
                                      10
                   5
 Pro Arg His Pro Pro Pro Leu His Ala Ala Leu Pro Ile Val Thr Ser
                                  25
 Thr Ala Ser Thr Thr Thr Ala Ile Thr Thr Gln Thr Ile Arg Ser Thr
                              40
 Ile Ser Ser Thr Val Ile Val Pro His Ser His Ser Ser Asn Trp Ile
                          55
 Pro Xaa Ala Xaa Pro Gly Leu Phe Xaa Lys Arg Lys
                      70
 <210> 29
 <211> 294
 <212> DNA
 <213> Homo sapiens
```

<220> <221> unsure <222> (20)

<220>

<221> unsure

<222> (23)

<220>

<221> unsure

<222> (28)

<220>

<221> unsure

<222> (46)

<220>

<221> unsure

<222> (64)

<220>

<221> unsure

<222> (66)

<220>

<221> unsure

<222> (69)

<220>

<221> unsure

<222> (86)

<220>

<221> unsure

<222> (92)

<220>

<221> unsure

<222> (101)

<220>

<221> unsure

<222> (103)

<220>

<221> unsure

<222> (107)

<220>

<221> unsure

<222> (185)

<220>

<221> unsure

<222> (208)

<220>

<221> unsure

<222> (214)

```
<400> 29
taaaaacccc tttttcctcn tangggtnta tcatagggtc ccggtngctg tcccagcaat 60
tttntnggng gatcataaaa tccttngatt tnactcgtga nanttgngaa gatctcaata 120
tacctattta aaaatgtttt aaggtacagg tttcagcata aatgtattag tgtaaattag 180
atacngggca aaatgcagta agtttttnta tatntagata cataacccaa tttaaattgc 240
ctaaatacac cgtaagttaa cagtttaaac ctacaaactt aattaagcgg ccgc
<210> 30
<211> 514
<212> DNA
<213> Homo sapiens
<220>
<221> unsure
<222> (462)
<220>
<221> unsure
<222> (467)
<220>
<221> unsure
<222> (481)
<400> 30
aagettggea egtggetgat tggagetgta aaacateate aggtgttget attwittitat 60
atgattattc tgttacttgt atttattgtt cagttttctg tatcttgcgc ttgtttagcc 120
ctgaaccagg agcaacaggg tcagcttctg gaggttggtt ggaacaatac ggcaagtgct 180
cgaaatgaca tccagagaaa tctaaactgc tgtgggttcc gaagtgttaa cccaaatgac 240
acctgtctgg ctagctgtgt taaaagtgac cactcgtgct cgccatgtgc tccaatcata 300
ggagaatatg ctggagaggt tttgagattt gttggtggca ttggcctgtt cttcagtttt 360
acagagatec tggggtgttt ggctgaccta cagatacagg aaccagaaag acceccgcgc 420
gaatcctagt gcattccttt ggatgaggaa aacaagggaa gnttccnttt cgtattatgg 480
ncttgtttca ctttctgtaa tttttctgtt aagg
<210> 31
<211> 151
<212> PRT
<213> Homo sapiens
<220>
<221> UNSURE
<222> (123)
<220>
<221> UNSURE
<222> (134)
<220>
<221>. UNSURE
<222> (136)
<220>
<221> UNSURE
<222> (141)
<400> 31
Met Ile Ile Leu Leu Leu Val Phe Ile Val Gln Phe Ser Val Ser Cys
                                     10
```

Ala Cys Leu Ala Leu Asn Gln Glu Gln Gln Gly Gln Leu Leu Glu Val 25 Gly Trp Asn Asn Thr Ala Ser Ala Arg Asn Asp Ile Gln Arg Asn Leu Asn Cys Cys Gly Phe Arg Ser Val Asn Pro Asn Asp Thr Cys Leu Ala Ser Cys Val Lys Ser Asp His Ser Cys Ser Pro Cys Ala Pro Ile Ile 70 Gly Glu Tyr Ala Gly Glu Val Leu Arg Phe Val Gly Gly Ile Gly Leu Phe Phe Ser Phe Thr Glu Ile Leu Gly Cys Leu Ala Asp Leu Gln Ile 105 Gln Glu Pro Glu Arg Pro Pro Arg Glu Ser Xaa Cys Ile Pro Leu Asp 120 Glu Glu Asn Lys Gly Xaa Phe Xaa Phe Val Leu Trp Xaa Cys Phe Thr 135 Phe Cys Asn Phe Ser Val Lys 150 <210> 32 <211> 204 <212> DNA <213> Homo sapiens <220> <221> unsure -<222> (53) <220> <221> unsure <222> (106) <220> <221> unsure <222> (111) <220> <221> unsure <222> (128) <400> 32 acgtagcaaa aagatatttg attatcttaa aaattgttaa ataccgtttt cangaaagtt 60 ctcagtattg taacagcaac ttgtcaaacc taagcatatt tgaatntgat ntcccataat 120 ttgaaatnga aatcgtatgg tgtggctctg tatattctgt taaaaaatta agggaccaga 180 aaccttaaaa aaaaaaaaaa aaaa <210> 33 <211> 391 <212> DNA <213> Homo sapiens

```
<220>
<221> unsure
<222> (5)
<220>
<221> unsure
<222> (20)
<220>
<221> unsure
<222> (336)
<400> 33
gaachtgggc cgcatgtath tottotatgg caacaagaco toggtgcagt tocagaattt 60
ctcacccact gtggttcacc cgggagacct ccagactcag ctggctgtgc agaccaagcg 120
cgtggcggcg caggtggacg gcggcgcgca ggtgcagcag gtgctcaata tcgagtgcct 180
gegggaette etgaegeece egetgetgte egtgegette eggtaeggtg gegeececea 240
ggccctcacc ctgaagctcc cagtgaccat caacaagttc ttccagccca ccgagatggc 300
ggcccaggat ttcttccagc gctggaagca gctgancctc cctcaacagg aggcgcagaa 360
aatcttcaaa gccaaccacc ccatggacgc a
<210> 34
<211> 126
<212> PRT
<213> Homo sapiens
<220>
<221> UNSURE
<222> (3)
<220>
<221> UNSURE
<222> (108)
<400> 34
Met Tyr Xaa Phe Tyr Gly Asn Lys Thr Ser Val Gln Phe Gln Asn Phe
                  5
                                    10
Ser Pro Thr Val Val His Pro Gly Asp Leu Gln Thr Gln Leu Ala Val
Gln Thr Lys Arg Val Ala Ala Gln Val Asp Gly Gly Ala Gln Val Gln
                            40
Gln Val Leu Asn Ile Glu Cys Leu Arg Asp Phe Leu Thr Pro Pro Leu
                         55
Leu Ser Val Arg Phe Arg Tyr Gly Gly Ala Pro Gln Ala Leu Thr Leu
Lys Leu Pro Val Thr Ile Asn Lys Phe Phe Gln Pro Thr Glu Met Ala
                                    90
                 85
Ala Gln Asp Phe Phe Gln Arg Trp Lys Gln Leu Xaa Leu Pro Gln Gln
            100
                                105
Glu Ala Gln Lys Ile Phe Lys Ala Asn His Pro Met Asp Ala
        115
                            120
```

```
<210> 35
<211> 177
<212> DNA
<213> Homo sapiens
<220>
<221> unsure
<222> (7)
<220>
<221> unsure
<222> (11)
<220>
<221> unsure
<222> (66)
<220>
<221> unsure
<222> (135)
<400> 35
cocctentee nttteccece caageacaga ggggagaggg gecagggaag tggatgttte 60
ttecenteec accecacet gttgtagecc etectacecc etececatec aggggetgtg 120
tattattgtg agcgnataaa cagagagacg ctaaaaaaaa aaaaaaaa aaaaaaa
<210> 36 ·
<211> 655
<212> DNA
<213> Homo sapiens
<220>
<221> unsure
<222> (5)
<220>
<221> unsure
<222> (27)
<220>
<221> unsure
<222> (29)..(30)
<220>
<221> unsure
<222> (153)
<220>
<221> unsure
<222> (431)
<220>
<221> unsure
<222> (610)
<220>
<221> unsure
<222> (638)
```

```
<220>
<221> unsure
<222> (655)
<400> 36
caatnataaa atgtcagctt ttaaggnann cctgtggaat atattttcca gcaataaaaa 60
gagatccagg cagatattta catagttgtc cctgaatctg tgaaaaaatg gcttcgacag 120
ctaaagaatg ctgggaaaat tcttctgtta atnaccagtt ctcacagtga ttactgtaga 180
cttctctgcg aatatattct tgggaatgat tttacagacc tttttgacat tgtgattaca 240
aatgcattga agcctggttt cttctcccac ttaccaagtc agagaccttt ccggacactc 300
gagaatgatg aggagcagga ggcactgcca tctctggata aacctggctg gtactcccaa 360
gggaacgctg tccacctcta tgaacttctg aagaaaatga ctggcaaacc tgaacccaag 420
gttstttatt nwtggtgwca gcatgcawtc agatattttc ccagctcgtc actatagtaa 480
ttggggagac agtcctcatc cgkggaagga actcagaggg ggatgaargg gcacgaggga 540
gttcagaggc cttgagggag ttcagagcct cttagaagaa ggaaagggaa attttgaggg 600
gaccaaaagn caaaaccttt aattatttca ttttaaanat gggggttttt ttttn
<210> 37
<211> 199
<212> PRT
<213> Homo sapiens
<220>
<221> UNSURE
<222> (32)
<220>
<221> UNSURE
<222> (123)
<220>
<221> UNSURE
<222> (125)
<220>
<221> UNSURE
<222> (127)
<220>
<221> UNSURE
<222> (131)
<220>
<221> UNSURE
<222> (140)..(141)
<220>
<221> UNSURE
<222> (149)
<220>
<221> UNSURE
<222> (166)
<220>
<221> UNSURE
<222> (180)
<220>
```

<221> UNSURE

<222> (185)

<220>

<221> UNSURE

<222> (193)..(194)

<400> 37

Lys Glu Ile Gln Ala Asp Ile Tyr Ile Val Val Pro Glu Ser Val Lys
1 5 10 15

Lys Trp Leu Arg Gln Leu Lys Asn Ala Gly Lys Ile Leu Leu Xaa  $20 \hspace{1.5cm} 25 \hspace{1.5cm} 30$ 

Thr Ser Ser His Ser Asp Tyr Cys Arg Leu Leu Cys Glu Tyr Ile Leu 35 40 45

Gly Asn Asp Phe Thr Asp Leu Phe Asp Ile Val Ile Thr Asn Ala Leu 50 55 60

Lys Pro Gly Phe Phe Ser His Leu Pro Ser Gln Arg Pro Phe Arg Thr 65 70 75 80

Leu Glu Asn Asp Glu Glu Glu Glu Ala Leu Pro Ser Leu Asp Lys Pro 85 90 95

Gly Trp Tyr Ser Gln Gly Asn Ala Val His Leu Tyr Glu Leu Lys 100 105 110

Lys Met Thr Gly Lys Pro Glu Pro Lys Val Xaa Tyr Xaa Trp Xaa Gln 115 120 125

His Ala Xaa Arg Tyr Phe Pro Ser Ser Ser Leu Xaa Xaa Leu Gly Arg 130 135 140

Gln Ser Ser Ser Xaa Glu Gly Thr Gln Arg Gly Met Lys Gly His Glu 145 150 155 160

Gly Val Gln Arg Pro Kaa Gly Ser Ser Glu Pro Leu Arg Arg Lys 165 170 175

Gly Lys Phe Xaa Gly Asp Gln Lys Xaa Lys Pro Leu Ile Ile Ser Phe 180 185 190

Xaa Xaa Trp Gly Phe Phe Phe 195

<210> 38

<211> 265

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (11)

<220>

<221> unsure

.<222> (47)

```
<220>
<221> unsure
<222> (49)
<400> 38
tectecactg ntettateaa gtgatgagae actgatatee aaataantng tatttactga 60
aaaatgaagt gaagacccat atatgcagtt aaaaaaaagt taattttcaa aaaatactgt 120
aaaagacttt aaggaacaag ttttattgac caataagttg atatttgtcc ataggtctcc 180
tttctataaa tcatcttgat gtttaacaac tcttattata ttaaaatctc agtatcctaa 240
aacttaaaaa aaaaaaaaaa aaaaa
<210> 39
<211> 377
<212> DNA
<213> Homo sapiens
<400> 39
gaatteggea egaggattet cateagettt teetgggttt geeaattaca teegagetgg 60
gactictaatic atggetetge atgactette egattacetg etggakteag ceaagatgit 120
taactacgcg ggatggaaga acacctgcaa caacatcttc atcgtcttcg ccattgtttt 180
tatcatcacc cgactggtca tectgeeett etggateetg cattgeacce tgggtgtace 240
cactggaget ctatectgee ttetttggge tattacttet tteaatteea tgatgggagt 300
totacagoty otgoatatot totgggsota cotoatttty ogsatgggoo cacaagttoa 360
taactgggaa agctggt
<210> 40
<211> 102
<212> PRT
<213> Homo sapiens
<220>
<221> UNSURE
<222> (12)
<220>
<221> UNSURE
<222> (86)
<400> 40
Met Ala Leu His Asp Ser Ser Asp Tyr Leu Leu Xaa Ser Ala Lys Met
                                     10
Phe Asn Tyr Ala Gly Trp Lys Asn Thr Cys Asn Asn Ile Phe Ile Val
             20
                                 25
Phe Ala Ile Val Phe Ile Ile Thr Arg Leu Val Ile Leu Pro Phe Trp
                             40
Ile Leu His Cys Thr Leu Gly Val Pro Thr Gly Ala Leu Ser Cys Leu
Leu Trp Ala Ile Thr Ser Phe Asn Ser Met Met Gly Val Leu Gln Leu
                                         75
65
                     70
Leu His Ile Phe Trp Xaa Tyr Leu Ile Leu Arg Met Gly Pro Gln Val
                                     90
His Asn Trp Glu Ser Trp
```

100

```
<210> 41
<211> 359
<212> DNA
<213> Homo sapiens
<220>
<221> unsure
<222> (38)
<220>
<221> unsure
<222> (42)
<220>
<221> unsure
<222> (49)
<220>
<221> unsure
<222> (82)
<220>
<221> unsure
<222> (106)
<220>
<221> unsure
<222> (111)
<220>
<221> unsure
<222> (125)
<220>
<221> unsure
<222> (127)
<220>
<221> unsure
<222> (138)
<220>
<221> unsure
<222> (175)
<220>
<221> unsure
<222> (229)
<220>
<221> unsure
<222> (246)
<220>
<221> unsure
<222> (263)
<220>
```

<221> unsure

```
<222> (268)
<220>
<221> unsure
<222> (273)
<220>
<221> unsure
<222> (276)
<220>
<221> unsure
<222> (278)
<220>
<221> unsure
<222> (281)
<220>
<221> unsure
<222> (302)
<220>
<221> unsure
<222> (314)..(316)
<400> 41
aaaaagtggg ggctgtactg gggactgctc ggatgatntt tnttagtgnt actttttca 60
getgteeetg tagegacagg thtaagatet gactgeetee tttttntgge ntetteeece 120
ttccntnttc tcttcagnta ggctagctgg tttggagtag aatggcaact aattntaatt 180
tttatttatt aaatatttgg ggttttggtt ttaaagccag aattacggnt agcacctagc 240
atttengeag agggaceatt ttngacenaa atntantntt natgggtttt tttttaaaat 300
<210> 42
<211> 332
<212> DNA
<213> Homo sapiens
<400> 42
gaatteggea egagettgat tgeteeaggg cecacaaegg eagtgteeta catgteggtg 60
aaatgtgtgg atgcccgtaa gaaccatcac aagacaaaat ggttcgtgcc ttggggaccc 120
aatcattgtg acaagatccg agacattgaa gaggcaattc caagggaaat tgaagccaat 180
gacategtgt tttetgttea cattececte ecceacatgg gagatgagte ettggtteea 240
attcatgmtg tttatcctgg cagctgggac attgcctttc aagctaaaca accaaatcag 300
gggaaaatge aggaagtete catgggacgt tt
                                                               332
<210> 43
<211> 110
<212> PRT
<213> Homo sapiens
<220>
<221> UNSURE
<222> (83)
Glu Phe Gly Thr Ser Leu Ile Ala Pro Gly Pro Thr Thr Ala Val Ser
 1
                 5
                                   10
```

```
'Tyr Met Ser Val Lys Cys Val Asp Ala Arg Lys Asn His His Lys Thr
            20
                                25
Lys Trp Phe Val Pro Trp Gly Pro Asn His Cys Asp Lys Ile Arg Asp
                            40
                                               45
Ile Glu Glu Ala Ile Pro Arg Glu Ile Glu Ala Asn Asp Ile Val Phe
Ser Val His Ile Pro Leu Pro His Met Gly Asp Glu Ser Leu Val Pro
                    70
Ile His Xaa Val Tyr Pro Gly Ser Trp Asp Ile Ala Phe Gln Ala Lys
                85
Gln Pro Asn Gln Gly Lys Met Gln Glu Val Ser Met Gly Arg
                               105
<210> 44
<211> 314
<212> DNA
<213> Homo sapiens
<220>
<221> unsure
<222> (78)..(79)
<220>
<221> unsure
<222> (85)..(86)
<220>
<221> unsure
<222> (126)
<400> 44
tcactcctaa tccatgacca ctgttttttt cctatttata tcaccaggta gcctactgag 60
ttaatattta agttgtcnnt gggtnngtgt ccctgttttg tggcataata taactgaatt 120
teatgngaag atttatteea eeaggggtat tteagetttg aaaccaaate tgtgtateta 180
atactaacca atctgttgga tgtggatttt aaaaaatgtt tgctaaacta cccaagtaag 240
aaaaaaaaa aaaa
<210> 45
<211> 1089
<212> DNA
<213> Homo sapiens
<400> 45
gggctactac gatggcgatg agtttcgagt ggccgtggca gtatcgcttc ccacccttct 60
ttacgttaca accgaatgtg gacactcggc agaagcagct ggccgcctgg tgctcgctgg 120
tectgteett etgeegeetg cacaaacagt ecageatgac ggtgatggaa geteaggaga 180
gcccgctctt caacaacgtc aagctacagc gaaagcttcc tgtggagtcg atccagattg 240
tattagagga actgaggaag aaagggaacc tcgagtggtt ggataagagc aagtccagct 300
tectgateat gtggcggagg ccagaagaat gggggaaact catetateag tgggttteca 360
ggagtggcca gaacaactcc gtctttaccc tgtatgaact gactaatggg gaagacacag 420
aggatgagga gttccacggg ctggatgaag ccactctact gcggggctctg caggccctac 480
agcaggagea caaggccgag atcatcactg teagegatgg ccgaggegte aagttettet 540
ageagggace tgtetecett tacttettae eteccacett tecagggett teaaaaggag 600
```

```
acagacccag tgtcccccaa agactggatc tgtgactcca ccagactcaa aaggactcca 660
 gtcctgaagg ctgggacctg gggatgggtt tctcacaccc catatgtctg tcccttggat 720
 agggtgaggc tgaagcacca gggagaaaat atgtgcttct tctcgcccta cctcctttcc 780
 catcctagac tgtccttgag ccagggtctg taaacctgac actttatatg tgttcacaca 840
 tgtaagtaca tacacacatg cgcctgcagc acatgcttct gtctcctcct cctcccaccc 900 .
 ctttagctgc tgttgcctcc cttctcaggc tggtgctgga tccttcctag gggatggggg 960
 aagccctggc tgcaggcagc cttccaggca atatgaagat aggaggccca cgggcctggc 1020
 agtgagaggt gtggccccac accgatttat gatattaaaa tctcaactcc caaaaaaaaa 1080
 aaaaaaaa
 <210> 46
 <211> 176
 <212> PRT
 <213> Homo sapiens
 <400> 46
 Met Ala Met Ser Phe Glu Trp Pro Trp Gln Tyr Arg Phe Pro Pro Phe
                                     10.
 Phe Thr Leu Gln Pro Asn Val Asp Thr Arg Gln Lys Gln Leu Ala Ala
     20
                                 25
 Trp Cys Ser Leu Val Leu Ser Phe Cys Arg Leu His Lys Gln Ser Ser
                              40
 Met Thr Val Met Glu Ala Gln Glu Ser Pro Leu Phe Asn Asn Val Lys
                          55
 Leu Gln Arg Lys Leu Pro Val Glu Ser Ile Gln Ile Val Leu Glu Glu
  65
                      70
                                          75
 Leu Arg Lys Lys Gly Asn Leu Glu Trp Leu Asp Lys Ser Lys Ser Ser
 Phe Leu Ile Met Trp Arg Arg Pro Glu Glu Trp Gly Lys Leu Ile Tyr
            100
                                105
 Gln Trp Val Ser Arg Ser Gly Gln Asn Asn Ser Val Phe Thr Leu Tyr
                            120
                                                 125
 Glu Leu Thr Asn Gly Glu Asp Thr Glu Asp Glu Glu Phe His Gly Leu
Asp Glu Ala Thr Leu Leu Arg Ala Leu Gln Ala Leu Gln Glu His
 Lys Ala Glu Ile Ile Thr Val Ser Asp Gly Arg Gly Val Lys Phe Phe
                 165
                                     170
<210> 47
<211> 632
<212> DNA
<213> Homo sapiens
<400> 47
agcttcggaa taataatttt ggcaaatcta tcttctgaac cactcatttc tgtggtctta 60
atggetecaa titggggace aataatgite attgteteag gatecetgie aartgeagea 120
ggagtgaaac ctacaaaaag cctgatcatc agcagtctaa ctctgaacac tatcacctct 180
gtgttggctg caactgcaag cataatgggt gtagtcagtg tggctgtggg ttcacagttt 240
```

```
cogtttcggt ataattatac aatcaccaag ggtttggata ttttgatgtt aattttaaat 300
atgctagaat tetgcattgc tgtgtecate tetgettttg gatgtaaage tteetgttgt 360
aactocageg aggttettgt agtgetacea teaaateetg etgtgaetgt gatggeaece 420
cccacaccac ttaatgaagg tttgaggcca ccaaaagatc aacagacaaa tgctccagaa 480
atctatgctg actgtgacac aagaagcctc acatgaagaa attaccagta tccaacttcg 540
atactgatag acttgttgat attattatta tatgtaatcc aattatgaac tgtgtgtgta 600
tagagagata ataaattcaa aattatgttc tc
<210> 48
<211> 151
<212> PRT
<213> Homo sapiens
<400> 48
Met Ala Pro Ile Trp Gly Pro Ile Met Phe Ile Val Ser Gly Ser Leu
                                    10
Ser Ile Ala Ala Gly Val Lys Pro Thr Lys Ser Leu Ile Ile Ser Ser
                      25
            20
Leu Thr Leu Asn Thr Ile Thr Ser Val Leu Ala Ala Thr Ala Ser Ile
                            40
Met Gly Val Val Ser Val Ala Val Gly Ser Gln Phe Pro Phe Arg Tyr
                     55
Asn Tyr Thr Ile Thr Lys Gly Leu Asp Ile Leu Met Leu Ile Leu Asn
                    70
Met Leu Glu Phe Cys Ile Ala Val Ser Ile Ser Ala Phe Gly Cys Lys
                                    90
Ala Ser Cys Cys Asn Ser Ser Glu Val Leu Val Leu Pro Ser Asn
           100
                               105
Pro Ala Val Thr Val Met Ala Pro Pro Thr Pro Leu Asn Glu Gly Leu
                          120
Arg Pro Pro Lys Asp Gln Gln Thr Asn Ala Pro Glu Ile Tyr Ala Asp
    130
                     135
Cys Asp Thr Arg Ser Leu Thr
145
                   150
<210> 49
<211> 365
<212> DNA
<213> Homo sapiens
<220>
<221> unsure
<222> (18)
<220>
<221> unsure
<222> (25)
<220>
<221> unsure
```

<221> unsure <222> (5)

90

Pro Ile Val His Arg Val Ile Lys Val His Glu Lys Asp Asn Gly Asp

Ile Lys Phe Leu Thr Lys Gly Asp Asn Asn Glu Val Asp Asp Arg Gly

105

100

```
Leu Tyr Lys Glu Gly Gln Asn Trp Leu Glu Lys Lys Asp Val Val Gly
       115
                          120
Arg Ala Arg Xaa Phe Leu Pro Tyr Val Gly Met Val Thr Ile Ile Met
                     135
Asn Asp Tyr Pro Lys Phe Xaa Tyr Ala Leu Leu Ala Val Met Gly Ala
                   150
                                       155
Tyr Val Leu Leu Lys Arg Glu Ser
              165
<210> 52
<211> 309
<212> DNA
<213> Homo sapiens
<400> 52
ctetecece eccetetete tetetetege atactaacta ggtttgactg tattactegt 60
accagattta aaattagact agccttgcca caacgcccta ctgagaggta ctgtcgaact 120
gtagacagca tgatgttctt tgatggtgaa agtctaaatc tggaccgtgt tcagagatac 180
caaatgatga ggctgaaaag gggaaagggg gttcttcagt ctcttcttct tcttctttt 240
attititit ccatgatgit tictctatgg ccagtgcaaa tggtgttgtc acccttgcat 300
gttgccaac
<210> 53
<211> 60
<212> PRT
<213> Homo sapiens
<400> 53
Met Met Phe Phe Asp Gly Glu Ser Leu Asn Leu Asp Arg Val Gln Arg
                                    10
Tyr Gln Met Met Arg Leu Lys Arg Gly Lys Gly Val Leu Gln Ser Leu
Leu Leu Leu Phe Ile Phe Phe Ser Met Met Phe Ser Leu Trp Pro
                            40
Val Gln Met Val Leu Ser Pro Leu His Val Ala Asn
                        55
                                            60
<210> 54
<211> 257
<212> DNA
<213> Homo sapiens
<220>
<221> unsure
<222> (97)
<220>
<221> unsure
<222> (170)
<220>
```

```
<221> unsure
<222> (222)
<400> 54
aggictictic ggittettet atateateat tittattatta tgicetaata taaagtaetg 60
gctcataggg ccagggtatt attatagaat attattntcg catgtaaaca aagatatctt 120
tgctttaaga tgtgagaaga aatgaattta ctttgtttgc attaagttan ggaagagttg 180
taatatatac tttaagaaag aagagaagaa aactagtatc tntaagcggt aaaaaaaaaa 240
aaaaaaaaa aaaaaaa
<210> 55
<211> 467
<212> DNA
<213> Homo sapiens
<220>
<221> unsure
<222> (32)
<220>
<221> unsure
<222> (84)
<220> . .
<221> unsure
<222> (87)
<220>
<221> unsure
<222> (89)
<220>
<221> unsure
<222> (96)
<220>
<221> unsure
<222> (149)
<220>
<221> unsure
<222> (246)
<220>
<221> unsure
<222> (248)
<220>
<221> unsure
<222> (250)..(251)
<400> 55
cacgaggatt gatttccatc ttgcctctcc anaaggcaaa accttagttt ttgaacaaag 60
aaaatcagat ggagttcaca ctgntanana ctgaanttgg tgattacatg ttctgctttg 120
acaatacatt cagcaccatt tctgagaang tgattttctt tgaattaatc ctggataata 180
tgggagaaca ggcacaagaa caagaagatt ggaagaaata tattactggc acagatatat 240
tggatntnan nctggaagac atcctggaat ccatcaacag catcaagtcc agactaagca 300
aaagtgggca catacaaact ctgcttagag catttgaagc tcgtgatcga aacatacaag 360
aaagcaactt tgatagagtc aatttetggt ctatggttaa tttagtggtc atggtggtgg 420
tgtcagccat tcaagtttat atgctgaaga gtctgtttga agataag
```

```
<210> 56
<211> 133
<212> PRT
<213> Homo sapiens
<220>
<221> UNSURE
<222> (6)..(7)
<220>
<221> UNSURE
<222> (10)
<220>
<221> UNSURE
<222> (27)
<220>
<221> UNSURE
<222> (60)..(61)
<400> 56
Met Glu Phe Thr Leu Xaa Xaa Thr Glu Xaa Gly Asp Tyr Met Phe Cys
Phe Asp Asn Thr Phe Ser Thr Ile Ser Glu Xaa Val Ile Phe Phe Glu
                      · 25
Leu Ile Leu Asp Asn Met Gly Glu Gln Ala Gln Glu Glu Asp Trp
                            40
Lys Lys Tyr Ile Thr Gly Thr Asp Ile Leu Asp Xaa Xaa Leu Glu Asp
    50
                        55
Ile Leu Glu Ser Ile Asn Ser Ile Lys Ser Arg Leu Ser Lys Ser Gly
                    70
His Ile Gln Thr Leu Leu Arg Ala Phe Glu Ala Arg Asp Arg Asn Ile
                85
                                   90
Gln Glu Ser Asn Phe Asp Arg Val Asn Phe Trp Ser Met Val Asn Leu
                             105
Val Val Met Val Val Val Ser Ala Ile Gln Val Tyr Met Leu Lys Ser
                         120
       115
Leu Phe Glu Asp Lys
   130
```

<210> 57 <211> 387 <212> DNA <213> Homo sapiens

<220>
<221> unsure
<222> (48)

```
<220>
<221> unsure
<222> (113)
<220>
<221> unsure
<222> (116)
<220>
<221> unsure
<222> (178)
<400> 57
tgtttgaaga taagaggaaa agtagaactt aaaactccaa actagagnac gtaacattga 60
aaaatgaggc ataaaaatgc aataaactgt tacagtcaag accattaatg gtnttntcca 120
aaatattttg agatataaaa gtaggaaaca ggtataattt taatgtgaaa attaagtntt 180
cactttctgt gcaagtaatc ctgctgatcc agttgtactt aagtgtgtaa caggaatatt 240
ttgcagaata taggtttaac tgaatgaagc catattaata actgcatttt cctaactttg 300
aaaaattttq caaatqtctt aggtgattta aataaatgag tattgggcct aattgcaaaa 360
aaaaaaaaa aaaaaaaaa aaaaaaa
<210> 58
<211> 1150
<212> DNA
<213> Homo sapiens
<400> 58
ggegggtgac atteageegg eggttegggg egaeggaete tecatteeag aaecatggee 60
caatttgtcc gtaaccttgt ggagaagacc ccggcgctgg tgaacgctgc tgtgacttac 120
tegaageete gattggeeae attttggtae taegeeaagg ttgagetggt teeteecace 180
cctgctgaga tccctagagc tattcagagc ctgaaaaaaa tagtcaatag tgctcagact 240
ggtagettea aacageteae agttaaggaa getgtgetga atggtttggt ggeeaetgag 300
gtgttgatgt ggttttatgt cggagagatt ataggcaagc ggggcatcat tggctatgat 360
gtttgaagac caatctttaa catctgatta tatttgattt attatttgag tgttgttgga 420
ccatgtgtga tcagactgct atctgaataa aataagattt gtcaaaactc agtgttttct 480
ccatcagaca ctccatgaaa ggtcacaatt tctcttgata ttaagctggg ttgtctttaa 540
acaaccctaa atacacgtct gtttagcccg caattggaaa ggatatatgt ggcaatatta 600
acctggtaca tgaatatatg gggataacat tttaatttga aggtttggaa tatatatatt 660
taagetttat ttecagaaca gtgagggtta ggtettggga aaactataac ttgecaaagt 720
agaagaaata gtagtaccat atgccaaagt gatagagatg aatcatgtca gtagttagaa 780
taacatttca actqttttct ttqctaaaat cacagaaaga ccctattgac aacatctatg 840
tctgtaaaaa tgttagagta cttgtcatct tgaatatagc ctccccaaga gagaacaggg 900
tggtattcta agtatgtttc tttgtaacat ctttagcagt aggacagatc catacatgtg 960
aaatctgatt tttatgtgtg ttattcgttt gtctggtttt actacctttg caaaaacaaa 1020
ataccccaaa gatatttaaa caaggttata atttagcatc ttccctggat ctaaatagta 1080
aaaaaaaaa
<210> 59
<211> 103
<212> PRT
<213> Homo sapiens
<400> 59
Met Ala Gln Phe Val Arg Asn Leu Val Glu Lys Thr Pro Ala Leu Val
                                   10
Asn Ala Ala Val Thr Tyr Ser Lys Pro Arg Leu Ala Thr Phe Trp Tyr
```

25

Tyr Ala Lys Val Glu Leu Val Pro Pro Thr Pro Ala Glu Ile Pro Arg 40 Ala Ile Gln Ser Leu Lys Lys Ile Val Asn Ser Ala Gln Thr Gly Ser 55 Phe Lys Gln Leu Thr Val Lys Glu Ala Val Leu Asn Gly Leu Val Ala 70 Thr Glu Val Leu Met Trp Phe Tyr Val Gly Glu Ile Ile Gly Lys Arg 85 Gly Ile Ile Gly Tyr Asp Val 100 <210> 60 <211> 456 <212> DNA <213> Homo sapiens <220> <221> unsure <222> (269) <220> <221> unsure <222> (271) <400> 60 agagattcag gacctgcaga gtcgccagaa gcatgaaatt gaatctttgt atactaaact 60 gggcaaggtt ccccctgctg tcattattcc cccagctgct cctctgtcgg ggagaagaag 120 gagacccact aaaagcaaag gcagcaagtc tagtcgcagc agctcattgg gcaataaaag 180 cccacagett teaggeaace tgtetggtea gagtggaact teagtettae acccccaaca 240 gaccetecae cetectggea acateceana nteegggeag aateagetgt tacageeeet 300 taagccatct ccctccagtg acaacctcta ttcagccttc accagtgatg gtgccatttc 360 agtaccaage etttetgete caggteaagg aaccageage acaaacactg ttggggeaac 420 agtgaacage caageegeee aageteagee teetge <210> 61 <211> 130 <212> PRT <213> Homo sapiens <220> <221> UNSURE <222> (79)..(80) <400> 61 Met Lys Leu Asn Leu Cys Ile Leu Asn Trp Ala Arg Phe Pro Leu Leu 1 5 10 Ser Leu Phe Pro Gln Leu Leu Cys Arg Gly Glu Glu Gly Asp Pro 25 Leu Lys Ala Lys Ala Ala Ser Leu Val' Ala Ala Ala His Trp Ala Ile 40 Lys Ala His Ser Phe Gln Ala Thr Cys Leu Val Arg Val Glu Leu Gln 50 55

```
Ser Tyr Thr Pro Asn Arg Pro Ser Thr Leu Leu Ala Thr Ser Xaa Xaa
                    70
                                        75
Pro Gly Arg Ile Ser Cys Tyr Ser Pro Leu Ser His Leu Pro Pro Val
                                     90
Thr Thr Ser Ile Gln Pro Ser Pro Val Met Val Pro Phe Gln Tyr Gln
            100
                                105
Ala Phe Leu Leu Gln Val Lys Glu Pro Ala Ala Gln Thr Leu Leu Gly
       115
                            120
                                                125
Gln Gln
    130
<210> 62
<211> 188
<212> DNA
<213> Homo sapiens
<220>
<221> unsure
<222> (24)..(25)
<220>
<221> unsure
<222> (171)
<400> 62
taccetgece testeettt tttnnacece testettttt attititett tgetetttag 60
aacccagtga aaaataccag ggtactgggg tgcaactctt tcttatgata ggtcattagt 120
gctttaagca aaagatatta gcagctttga ctgcagcatt agcaattagg naaaaaaaaa 180
aaaaaaa
<210> 63
<211> 752
<212> DNA
<213> Homo sapiens
<220>
<221> unsure
<222> (151)
<220>
<221> unsure
<222> (616)
<220>
<221> unsure
<222> (636)
<220>
<221> unsure
<222> (662)
<220>
<221> unsure
<222> (711)
```

```
<220>
<221> unsure
<222> (722)
<400> 63
cottatggcc tactttaaaa aaaaaccaat accaaagaag cotacaatgt tggccttagc 60
caaaattctg ttgatttcaa cgttgtttta ttcacttcta tcggggagcc atggaaaaga 120
aaatcaagac ataaacacaa cacagaacat ngcagaagtt tttaaaaacaa tggaaaataa 180
acctatttct ttggaaagtg aagcaaactt aaactcagat aaagaaaata taaccacctc 240
aaatctcaag gcgagtcatt cccctccttt gaatctaccc aacaacagcc acggaataac 300
agatttctcc agtaactcat cagcagagca ttctttgggc agtctaaaac ccacatctac 360
catttecaca agreeteect tgatecatag ctttgtttct aaagtgeett ggaatgeace 420
tatagcagat gaagatettt tgcccatete agcacatece aatgstacae etgetetgty 480
ttcaraaaac ttcacttggt ctttgtcaat gacaccgtga aaactcctga taacagttcc 540
attacagtta gcatcetety ttcaraacca acttetecat etgtgacece ettgatagtg 600
gaaccaagtg gatggnttac cacaaacagt gatagnttca ctgggtttac cccttatcaa 660
gnaaaaacaa ctttacagcc taccttaaaa ttcaccaata attcaaaaact ntttccaaat 720
angtcagatc ccccaaaaaa aaaaaaaaaa aa
<210> 64
<211> 157
<212> PRT
<213> Homo sapiens
<220>
<221> UNSURE
<222> (35)
<220>
<221> UNSURE
<222> (140)
<220>
<221> UNSURE
<222> (145)
<220>
<221> UNSURE
<222> (147)
<400> 64
Met Leu Ala Leu Ala Lys Ile Leu Leu Ile Ser Thr Leu Phe Tyr Ser
Leu Leu Ser Gly Ser His Gly Lys Glu Asn Gln Asp Ile Asn Thr Thr
             20
Gln Asn Xaa Ala Glu Val Phe Lys Thr Met Glu Asn Lys Pro Ile Ser
         35
                             40
Leu Glu Ser Glu Ala Asn Leu Asn Ser Asp Lys Glu Asn Ile Thr Thr
                         55
Ser Asn Leu Lys Ala Ser His Ser Pro Pro Leu Asn Leu Pro Asn Asn
                     70
                                         75
Ser His Gly Ile Thr Asp Phe Ser Ser Asn Ser Ser Ala Glu His Ser
```

90

85

95

Leu Gly Ser Leu Lys Pro Thr Ser Thr Ile Ser Thr Ser Pro Pro Leu 105 100 110 Ile His Ser Phe Val Ser Lys Val Pro Trp Asn Ala Pro Ile Ala Asp 120 Glu Asp Leu Pro Ile Ser Ala His Pro Asn Xaa Thr Pro Ala Leu Xaa Ser Xaa Asn Phe Thr Trp Ser Leu Ser Met Thr Pro 150 145 155 <210> 65 <211> 417 <212> DNA <213> Homo sapiens <221> unsure <222> (69) <400> 65 aagettggea egaggtettt agaagaacta caaaacetga atggaaaact tegaagtgaa 60 ggacaaggna atatgggctt tactaggcag aatcacaggg cagaagttga atataccggc 120 aattttgaga gcacccaagg agagaaaacc aagtaaaaaa agaaggagyc acacaaaaga 180 catctactct tcctgcagta ctttatagtt gtgggatttg taagaagaac catgatcagc 240 atcttctttt attgtgtgat acctgtaaac tacattacca ttttggatgt ctggatcctc 300 ctctaacaag gatgccaaga aagacccaaa acagttattg gcagtgctcg gaatgtgacc 360 aggcagggag cagtgacatg gaagcagata tggccatgga aaccctacca gatggaa <210> 66 <211> 35 <212> PRT <213> Homo sapiens <400> 66 Met Pro Arg Lys Thr Gln Asn Ser Tyr Trp Gln Cys Ser Glu Cys Asp 5 10 Gln Ala Gly Ser Ser Asp Met Glu Ala Asp Met Ala Met Glu Thr Leu Pro Asp Gly 35 <210> 67 <211> 359 <212> DNA <213> Homo sapiens <220> <221> unsure <222> (90) <220> <221> unsure <222> (156)..(157)

```
<220>
<221> unsure
<222> (160)
<400> 67
tctgtgttca gtataatttt atttttctca accttaaata tgaacttagg aaataaggag 60
ggaagtacaa agattattga ctatacaacn taccagctga aagaaagatc ttcatcaaca 120
totgtatott tocagaggta tacagaatta aaattnnatn ttoaagottt aatgatocag 180
ttttaagtca acggcagaag tatgttgaat atttcatcac tcaatcttga actgatttag 240
aagagactct ttgctgaaat tgaattgcac ttatacatgt aaattgtcaa catgtaattt 300
<210> 68
<211> 656
<212> DNA
<213> Homo sapiens
<400> 68
aacgaacggc ttgggcgcgg actggtatcc ggggactgtg acttgcaggg tccgccatgg 60
agccagagca gatgctggag ggacaaacgc aggttgcaga aaatcctcac tctgagtacg 120
gtctcacaga caacgttgag agaatagtag aaaatgagaa gattaatgca gaaaagtcat 180
caaaqcagaa ggtagatete cagtetttge caactegtge ctacetggat cagacagttq 240
tgcctatctt attacaggga cttgctgtgc ttgcaaagga aagaccacca aatcccattg 300
aatttctagc atcttatctt ttaaaaaaca aggcacagtt tgaagatcga aactgactta 360
atgggaagaa cagaaaaatt tagttgctac tgtagattta catgattaag aggcagcttt 420
aattgccatg atcattccct ctttttggat gtataagaac cttccggaca acagaaccta 480
tttctggaat tgcagaagat aacatatttc ccttattttg atttaatcac cataaaccat 540
acctatttaa tgagtgtatt ctgtgcaatt tttttctcag attgtcttta actttgtttt 600
taaaatgacc ttcaaaataa actgtcaaaa caccattaaa aaaaaaaaa aaaaaa
<210> 69
<211> 99
<212> PRT
<213> Homo sapiens
<400> 69
Met Glu Pro Glu Gln Met Leu Glu Gly Gln Thr Gln Val Ala Glu Asn
                                 10
                 5
Pro His Ser Glu Tyr Gly Leu Thr Asp Asn Val Glu Arg Ile Val Glu
            20
                               25
Asn Glu Lys Ile Asn Ala Glu Lys Ser Ser Lys Gln Lys Val Asp Leu
                           40
Gln Ser Leu Pro Thr Arg Ala Tyr Leu Asp Gln Thr Val Val Pro Ile
                       55
Leu Leu Gln Gly Leu Ala Val Leu Ala Lys Glu Arg Pro Pro Asn Pro
Ile Glu Phe Leu Ala Ser Tyr Leu Leu Lys Asn Lys Ala Gln Phe Glu
                                 90
Asp Arg Asn
```

45

<210> 70 <211> 979

```
<212> DNA
<213> Homo sapiens
<400> 70
ggtttggtga ggaaattacc agagaactat taaagacttg gatgctcttc tcggctttgc 60
tattaagtaa gttggacaag ttgtttggct tctttgagcc tctgttttct ccattctaaa 120
attotaaaat gggagtgttg aattagatca gtggctttcg aactttctgc tcctagtagt 180
gagaaataca ttttactcca ctccctggta tgtacacgca ttcctgtgtt ttgtgaaaac 240
ctgacaccat geteeteet cactacatgt aaaacacttt tatteattaa aaagaaaact 300
gactggcttg gacctacaaa ttagtttcat tatttgttaa tgtttgaaag ccattaaaag 360
atgaatatta aggtttcttt atactcaata cttgtagttt tgtttggggg aatgagagga 420
tgcccttggt acctttgtga ggcctctcca ctgagggtca atcatgactt ctgttttaaa 480
ccagcccatc ccatcttctc cagctgctct ccttatgtct tgcttctctc ccctccaacc 540
ttctcagcat aaggactcaa tcctaggctc ctaccccaga cgggtgcctt ccaacgttcc 600
tggtgccagt ggccccccat cagccatgtt cccccagecc cttctccaca ctcttgtcac 660
ccagggcccc atccttcagt gcattgcaca ctttgcatgc tgggtcaggg aagattgtgg 720
agagaggaca gtgcacctgg tttcccccac atagactgcg tgggggtatg tcctgcttcc 780
gecaetteca actgtggcae ttgggcaege eceteteagg geaeetteee tttttgttte 840
cycaaaatga gyttytaata ytycctyccy cactytctyy cacacaytaa yctctcaaga 900
aatgttaget gttgttgeeg ttagaacace atagetagaa taccatacet ggeatteact 960
taaaaaaaa aaaaaaaaa
<210> 71
<211> 96
<212> PRT
<213> Homo sapiens
<400> 71
Met Thr Ser Val Leu Asn Gln Pro Ile Pro Ser Ser Pro Ala Ala Leu
Leu Met Ser Cys Phe Ser Pro Leu Gln Pro Ser Gln His Lys Asp Ser
Ile Leu Gly Ser Tyr Pro Arg Arg Val Pro Ser Asn Val Pro Gly Ala
         35
                             40
Ser Gly Pro Pro Ser Ala Met Phe Pro Gln Pro Leu Leu His Thr Leu
Val Thr Gln Gly Pro Ile Leu Gln Cys Ile Ala His Phe Ala Cys Trp
65
                     70
                                         75
Val Arg Glu Asp Cys Gly Glu Arg Thr Val His Leu Val Ser Pro Thr
                                     90
<210> 72
<211> 310
<212> DNA
<213> Homo sapiens
<400> 72
attgaggaaa accacaaaaa acttcaaaac agctacaacg ggaaaaagag agttttgtcc 60
cacagtcagc aggccactag tttattaact tccagtcacc ttgatttttg ctaaaatgaa 120
gactetgeag tetacaette teetgttact gettgtgeet etgataaage cageaceace 180
aacccagcag gactcacgca ttatctatga ttatggaaca gataattttg aagaatccat 240
atttagccaa gattatgagg ataaatacct ggatggaaaa aatattaagg aaaaagaaac 300
totoataata
```

```
<210> 73
<211> 65
<212> PRT
<213> Homo sapiens
<400> 73
Met Lys Thr Leu Gln Ser Thr Leu Leu Leu Leu Leu Val Pro Leu
                                    10
Ile Lys Pro Ala Pro Pro Thr Gln Gln Asp Ser Arg Ile Ile Tyr Asp
             20
                                 25
Tyr Gly Thr Asp Asn Phe Glu Glu Ser Ile Phe Ser Gln Asp Tyr Glu
                            40
Asp Lys Tyr Leu Asp Gly Lys Asn Ile Lys Glu Lys Glu Thr Val Ile
 50 (
                       55
Ile
 65
<210> 74
<211> 303
<212> DNA
<213> Homo sapiens
<220>
<221> unsure
<222> (7)
<220>
<221> unsure
<222> (10)
<220>
<221> unsure
<222> (17)
<220>
<221> unsure
<222> (29)
<220>
<221> unsure
<222> (40)
<220>
<221> unsure
<222> (49)
<220>
<221> unsure
<222> (63)
<220>
<221> unsure .
```

<222> (65)

<220>

<221> unsure <222> (73) <220> <221> unsure <222> (78) <220> <221> unsure <222> (83) <220> <221> unsure <222> (88) <220> <221> unsure <222> (93) <220> <221> unsure <222> (130) <220> <221> unsure <222> (132) <220> <221> unsure <222> (153) <220> <221> unsure .<222> (155) <220> <221> unsure <222> (180) <220> <221> unsure <222> (200) <220> <221> unsure <222> (211) <220> <221> unsure <222> (241) <220> <221> unsure <222> (266) <220> <221> unsure <222> (279)

<400> 74

```
cccaagnaan titicaantit tigcctiinc iggcctitan iggatcccna aagcatttaa 60
ggmanatgtt ccnaaaantt tgnaaagnta aangtttccc atgatcgctc atttttttt 120
tatgattcan angttattcc ttataaagta agnantttgt tttcctccta tcaaggcagn 180
tattttatta aatttttcan ttagtttgag naatagcaga tagtttcata tttagggaaa 240
<210> 75
<211> 1823
<212> DNA
<213> Homo sapiens
<400> 75
qawaqcttqq cacgaggcac aagtagctac gactgcaagc acctgccacc ataaaggqct 60
gcattttgcc accataaagg gctgcatttt tttaaaaagc ctaggcagct ctaacatcat 120
ctgatatgga cacaaggcca acagtttcct tatttacatc cttacctcta aaagatactt 180
caaagtgaca aaaacgtgtt ccttccccac ttagagacaa tgattaacag ggccctatat 240
gttcttacca catacagagg atgcatttat ttttgctcta tgacacttgc aaaaatctct 300
actgtaatta atttgggtct attattaact ctctgttcca tcatagaatg tggccaggcc 360
ttacaatgga gagccagagt taaaacttca agttgcatct gtttttgggc tgagtcacca 420
cetttgeete atgeteettt gtetgeaaag geetaggatt etttettaa atgaaatget 480
taggactttg tggcttgtta catttgtcat ttaactgcag tgctattctt tgaaagctgc 540
tatgtgtatt ttctctgaag tctgcatttt actaaaattt acaacagtct gatgattgat 600
tgattactgt ccaggtacat tttagaaaaa gtgttcttct tccagtttgt tttactaagc 660
aaactttgag taaatccttt gtcctatatt gaatccagtc ccaaagtgtt caggtgagtt 720
tototagtto cataaacaaa acatacatag tgggaactco ctggtatgco atagagcaca 780
caagaacccc aatattaatg ctaacaatta taccagtcca ttttgtttat tctgtggaat 840
tgacttgaca aagcatgaag atattcccag tgtctgtctg ataatatttt gcatctaaga 900
atgggtttga ctcaagatct tgggttacca agatgtctta aatgttcagt aaatatcttt 960
cttacagtcc agtagcttag agcatgtttg ctgattgata ttacatttaa acttggggct 1020
acagettgtt acetagaatt ttgagatact aagagaatge aattttaaat geecaetggt 1080
tttatttgtt ttggagagag ggtctcattc tgtcacccag gctagagtac agtgggaaca 1140
gtcatggctc actgcagctt aagctcactg cctgggctca agtgatctta ctccagcctc 1200
ccaagcagct gggactacac caccacggt atgcaccacc atacctggct gatttttaaa 1260
attititicta gagatgaggi cicactatgi tgcccagcig gictcataci ccicagtica 1320
cgcattcctc ccacctccac ctcccaaact gctgggatta caggtgtgag ccaccatgcc 1380
caacacccac tgatctttaa ctctcacatg ttgggcataa gaagtcacta tataattgtt 1440
actggaaagc aagacttaac gaacaattct gactatgaaa aatgtctctt tcagtttgtt 1500
ctgtaaatat ttagaaaagt gacagctgtc aacytcagrg taactatttc taaaaatgta 1560
aatatgtatt aatccttgta tcttttatgg taattttgca tattgatatg aattatataa 1620
aattgtttaa aataaaaggt gtccttgaat tactgaccac ccatagatgt ctactgttac 1680
caggittiac aatgcaaatt ticactaata cctgggitta atacagetea catcactgaa 1740
tgttacacat gagtttaaat gggttaatat acaggttttg ttataataaa gttactgatt 1800
aaattaaaaa aaaaaaaaaa aaa
<210> 76
<211> 78
<212> PRT
<213> Homo sapiens
<400> 76
Met Ile Asn Arg Ala Leu Tyr Val Leu Thr Thr Tyr Arg Gly Cys Ile
 1
                                   10
Tyr Phe Cys Ser Met Thr Leu Ala Lys Ile Ser Thr Val Ile Asn Leu
Gly Leu Leu Thr Leu Cys Ser Ile Ile Glu Cys Gly Gln Ala Leu
      . 35
                            40
```

```
Gln Trp Arg Ala Arg Val Lys Thr Ser Ser Cys Ile Cys Phe Trp Ala
                          55
Glu Ser Pro Pro Leu Pro His Ala Pro Leu Ser Ala Lys Ala
                      70
<210> 77
<211> 583
<212> DNA
 <213> Homo sapiens
<220>
<221> unsure
<222> (5)
<220>
<221> unsure
<222> (217)
<400> 77
cacgngggtg aggecgactg etgaagacag etegecacce teettgeete caetecaate 60
caggggctgg ggccacattc tttgccttca tttatcctca gatcaggtga gatcgacagg 120
aggtgttgat ggcagtgcca gcaattattg ctaatccgtt tgcatcctta tgcatagatc 180
tgaattcaga ctttgtgaat ttccagaggt gtgggtnata taatagaatt cagtgagtgg 240
gcatggctga tcttgtgcaa attaaaagtt atggggcata agaatagcaa aagttgaact 300
tettttaaaa aggaaagtac cetgagagee agtattggtt gaggetette agtatgeeca 360
ggttggcagc actgagaacc gcaggaacgg cctgttgtta caaaaaggag attgactcag 420
ctgcccttgg tgcatctgac tgactatgac tgctgagaga ttccaaggac ccttaatgcc 480
agggctaacc tetecatgtg cagtgagace tetggaggaa gtgtcatect etggetttgt 540
gtggtactca ttatggtgca gtgcgggcat gaaatgaaga cac
<210> 78
<211> 29
<212> PRT
 <213> Homo sapiens
<400> 78
Met Cys Ser Glu Thr Ser Gly Gly Ser Val Ile Leu Trp Leu Cys Val
Val Leu Ile Met Val Gln Cys Gly His Glu Met Lys Thr
              20
<210> 79
<211> 311
<212> DNA
<213> Homo sapiens
<220>
<221> unsure
<222> (40)
<220>
<221> unsure
<222> (234)
<220>
<221> unsure
```

90

Gly Gly Ala Gly Gly Leu Arg Ser His Leu Xaa Ile Thr Asp Ser Ala

Gly His Ile Leu Tyr Ser Lys Glu Asp Ala Thr Lys Gly Lys Phe Ala

70

85

```
Phe Thr Thr Glu Asp Tyr Asp Met Phe Glu Val Cys Phe Glu Ser Lys
                               105
           100
Gly Thr Gly Arg Ile
       115
<210> 82
<211> 225
<212> DNA
<213> Homo sapiens
<220>
<221> unsure
<222> (42)
<220>
<221> unsure
<222> (61)
<220>
<221> unsure
<222> (71)
<220>
<221> unsure
<222> (99)
<400> 82
tettteaatt taeettgtga aaacaccett aactttttet tnaccettag etgaaatgtt 60
nacatagett neggegatat etteteatga tetetatatne ettaaaatgg egatggatgt 120
gacacctcat aaaagtgagc tttgaactgt agataactct taaagaaaat gtcattttag 180
<210> 83
<211> 1711
<212> DNA
<213> Homo sapiens
<400> 83
cgagggcagg tcagtcaggt tcctgggcgc tctgttacac aagcaagata cagccagecc 60
cacctaattt tgtttccctg gcaccctcct gctcagtgcg acattgtcac acttaaccca 120
totgttttot ctaatgcacg acagatteet ttcagacagg acaactgtga tatttcagtt 180
cctgattgta aatacctcct aagcctgaag cttctgttac tagccattgt gagcttcagt 240
ttottcatct gcaaaatggg cataatacaa totattottg ccacatcaag ggattgttat 300
tcctttaaaa aaaaaaccaa taccaaagaa gcctacaatg ttggccttag ccaaaattct 360
gttgatttca acgttgtttt attcacttct atcggggagc catggaaaag aaaatcaaga 420
cataaacaca acacagaaca ttcagaagtt tttaaaacaa tggaaaataa acctatttct 480
ttggaaagtg aagcaaactt aaactcagat aaagaaaata taaccacctc aaatctcaag 540
gegagteatt ecceteettt gaatetaece aacaacagee aeggaataac agatttetee 600
agtaactcgt cagcagagca ttctttgggc agtctaaaac ccacatctac catttccaca 660
agcoctcoot tgatccatag ctttgtttct aaagtgcott ggaatgcacc tatagcagat 720
gaagatottt tgcccatoto agcacatoco aatgotacao otgototgto ttcagaaaac 780
ttcacttggt ctttggtcaa tgacaccgtg aaaactcctg ataacagttc cattacagtt 840
agcatectet etteagaace aactteteea tetgtgaeee eettgatagt ggaaceaagt 900
ggatggctta ccacaaacag tgatagcttc actgggttta tcccttatca agaaaaaaca 960
actictacago otacottada atticaceaat aatticadaac totttocaaa taogtoagat 1020
ccccaaaaag aaaatagaaa tacaggaata gtattcgggg ccattttagg tgctattctg 1080
ggtgtctcat tgcttactct tgtgggctac ttgttgtgtg gaaaaaggaa aacggattca 1140
tttteecate ggegaettta tgacgacaga aatgaaccag ttetgegatt agacaatgea 1200
```

coggaacctt atgatgtgag ttttgggaat totagotact acaatccaac tttgaatgat 1260 tcagccatgc cagaaagtga agaaaatgca cgtgatggca ttcctatgga tgacatacct 1320 ccaettegta ettetgtata gaactaacag caaaaaggeg ttaaacagca agtgteatet 1380 acatoctage cttttgacaa attoatettt caaaaggtta cacaaaatta ctgtcacgtg 1440 gattttgtca aggagaatca taaaagcagg agaccagtag cagaaatgta gacaggatgt 1500 atcatccaaa ggttttcttt cttacaattt ttggccatcc tgaggcattt actaagtagc 1560 cttaatttgt attttagtag tattttctta gtagaaaata tttgtggaat cagataaaac 1620 taaaagattt caccattaca gccctgcctc ataactaaat aataaaaatt attccaccaa 1680 aaaattctaa aacaaaaaaa aaaaaaaaaa a <210> 84 <211> 361 <212> PRT <213> Homo sapiens <400> 84 Met Gly Ile Ile Gln Ser Ile Leu Ala Thr Ser Arg Asp Cys Tyr Ser 10 Phe Lys Lys Lys Thr Asn Thr Lys Glu Ala Tyr Asn Val Gly Leu Ser Gln Asn Ser Val Asp Phe Asn Val Val Leu Phe Thr Ser Ile Gly Glu 40 Pro Trp Lys Arg Lys Ser Arg His Lys His Asn Thr Glu His Ser Glu Val Phe Lys Thr Met Glu Asn Lys Pro Ile Ser Leu Glu Ser Glu Ala 70 Asn Leu Asn Ser Asp Lys Glu Asn Ile Thr Thr Ser Asn Leu Lys Ala 85 90 Ser His Ser Pro Pro Leu Asn Leu Pro Asn Asn Ser His Gly Ile Thr Asp Phe Ser Ser Asn Ser Ser Ala Glu His Ser Leu Gly Ser Leu Lys 120 Pro Thr Ser Thr Ile Ser Thr Ser Pro Pro Leu Ile His Ser Phe Val 130 135 140 Ser Lys Val Pro Trp Asn Ala Pro Ile Ala Asp Glu Asp Leu Leu Pro 150 155 Ile Ser Ala His Pro Asn Ala Thr Pro Ala Leu Ser Ser Glu Asn Phe 170 165 Thr Trp Ser Leu Val Asn Asp Thr Val Lys Thr Pro Asp Asn Ser Ser 185 Ile Thr Val Ser Ile Leu Ser Ser Glu Pro Thr Ser Pro Ser Val Thr 200 195 Pro Leu Ile Val Glu Pro Ser Gly Trp Leu Thr Thr Asn Ser Asp Ser 215

235

Phe Thr Gly Phe Ile Pro Tyr Gln Glu Lys Thr Thr Leu Gln Pro Thr

230

Leu Lys Phe Thr Asn Asn Ser Lys Leu Phe Pro Asn Thr Ser Asp Pro 250 Gln Lys Glu Asn Arg Asn Thr Gly Ile Val Phe Gly Ala Ile Leu Gly 265 Ala Ile Leu Gly Val Ser Leu Leu Thr Leu Val Gly Tyr Leu Leu Cys 280 Gly Lys Arg Lys Thr Asp Ser Phe Ser His Arg Arg Leu Tyr Asp Asp 295 Arg Asn Glu Pro Val Leu Arg Leu Asp Asn Ala Pro Glu Pro Tyr Asp 310 Val Ser Phe Gly Asn Ser Ser Tyr Tyr Asn Pro Thr Leu Asn Asp Ser 325 330 Ala Met Pro Glu Ser Glu Glu Asn Ala Arg Asp Gly Ile Pro Met Asp 345 Asp Ile Pro Pro Leu Arg Thr Ser Val 355 <210> 85 <211> 565 <212> DNA <213> Homo sapiens <400> 85 tttcagacca gcttgtgtca atagggtcct acagagcagc tgatatcagc agttttacta 60 gtatgcagga cctgaaagaa tatctcaaag ggaaaacaat gtttcataat gttcaggaag 120 ttatctatag agcagctaag gggaaataat cttgtaacag ggtctgggtg attctgaggt 180 aataggcccc aaacaaccat ggggaagcag gtcagagggc aagctggcct agtgtttaac 240 attgaatggg ctgaaagttt ggtttatttt tgtttcttgt ttctccccct cccttcttac 300 ctgaataatt ttatgaagtt tatagggatg gtttcaggac ctccattcta tctgttcctg 360 aaatattaca aaaagattat tattgtagca ctcatctaat tgtgttttat ctcgttgttt 420 gcatgtctgt ttcttcccca gtgagttgta aattgcttaa gggcaaacag acgcatccta 480 tttatctgtc tgtcactaac attaagcaca gcatttggta tacagtcatc actctaataa 540 agtttgaaaa aaaaaaaaaa aaaaa <210> 86 <211> 66 <212> PRT <213> Homo sapiens <400> 86 Met Gly Lys Gln Val Arg Gly Gln Ala Gly Leu Val Phe Asn Ile Glu 5 10 Trp Ala Glu Ser Leu Val Tyr Phe Cys Phe Leu Phe Leu Pro Leu Pro 25 Ser Tyr Leu Asn Asn Phe Met Lys Phe Ile Gly Met Val Ser Gly Pro 40 Pro Phe Tyr Leu Phe Leu Lys Tyr Tyr Lys Lys Ile Ile Ile Val Ala 55

```
Leu Ile
 65
<210> 87
<211> 636
<212> DNA
<213> Homo sapiens
<220>
<221> unsure
<222> (528)
<220>
<221> unsure
<222> (530)
<220°>
<221> unsure
<222> (580)
<400> 87
cacgagggaa aaaaagagtt tttttttag atcatcagct attgttagtg tttgtgtatg 60
ttatgtgtgg ctcaagacaa ctttgcttct tttaatatag gcagggaagt caaaagattg 120
gatatecetg etttataeca agaaagaeaa caceccacat ttgcagtgee tgaaaacaet 180
accagocato tgaaaaacat gtgacttota acttotgtto ttttttgtag cagtggaato 240
ccacggtgat atctgaggga tgtggttacc ttttggagga ggttgacggt ttctaaggat 300
gattetttet gagtgaaata ttgteagtgt cattgacett tteattattt caactattat 360
tattccaggt tatcaatact ctggctgacc atcatcatcg tgagactgac tttggtgtag 420
gagttcgaga ccaccctggc caacatggca aaaccccatc tccacaaaaa ttggataatt 480
tgataattat cattattggg tttctgagac gttacacatt taacattntn ttctgcacaa 540
gttgcctttg tgtgagtata ctaactttct gtagaggtan acttgtaatc acaaataaga 600
ataaattata taaaacaaaa aaaaaaaaaa aaaaaa
<210> 88
<211> 105
<212> PRT
<213> Homo sapiens
<220>
<221> UNSURE
<222> (76)
<220>
<221> UNSURE
<222> (93)
<400> 88
Phe Phe Leu Ser Glu Ile Leu Ser Val Ser Leu Thr Phe Ser Leu Phe
                  5
                                     10
Gln Leu Leu Phe Gln Val Ile Asn Thr Leu Ala Asp His His His
                                 25
             20
Arg Glu Thr Asp Phe Gly Val Gly Val Arg Asp His Pro Gly Gln His
                             40
        35
Gly Lys Thr Pro Ser Pro Gln Lys Leu Asp Asn Leu Ile Ile Ile Ile
    50
                         55
```

Ile Gly Phe Leu Arg Arg Tyr Thr Phe Asn Ile Xaa Phe Cys Thr Ser

70 75 Cys Leu Cys Val Ser Ile Leu Thr Phe Cys Arg Gly Xaa Leu Val Ile 90 Thr Asn Lys Asn Lys Leu Tyr Lys Thr 100 <210> 89 <211> 861 <212> DNA <213> Homo sapiens <400> 89 ggccggaggg cagatgactc tgagaagggc aagcacttta accttttaag cccaaccaga 60 tgagttgect geagttttgg aggeetteag ageattteae tagaeetetg tetgtgtegg 120 tccagtgtct ttagccaage tttgattaaa gatgacttcc ttgtttgctc aagaaattcg 180 cctttctaaa agacatgaag aaatagtatc acaaagatta atgttacttc aacaaatgga 240 gaataaattg ggtgatcaac acacagaaaa ggcatctcaa ctccaaactg ttgagactgc 300 ttttaaaagg aaccttagtc ttttaaagga tatagaagca gcagaaaagt cactacagac 360 caggattcac ccacttccac ggcctgaggt ggtttctctt gagactcgtt actgggcatc 420 agtagaagaa tatattccca aatgggaaca gtttctttta ggaagagcac catatccttt 480 tgctgttgaa aatcaaaatg aagcagaaaa taccattcaa aatgaggcac agcgataact 540 tettcacatg ctatttcaaa aageetgttt aataaagetg aatgttaagg tgtatgtagg 600 ttattgcagg aactttagga attaaatatg ttcatattct tcgattatct cctaagtgac 660 agtgaagata tgagaattta ctggcaagtc acatgttatc acctactact atttcaaggt 720 catgaatttg ctttctacca aacccataga tgtgttaaac acgaatatta aaaggtggac 780 aaaaaaaaa aaaaaaaaaa a <210> 90 <211> 128 <212> PRT <213> Homo sapiens <400> 90 Met Thr Ser Leu Phe Ala Gln Glu Ile Arg Leu Ser Lys Arg His Glu 10 Glu Ile Val Ser Gln Arg Leu Met Leu Leu Gln Gln Met Glu Asn Lys Leu Gly Asp Gln His Thr Glu Lys Ala Ser Gln Leu Gln Thr Val Glu 40 Thr Ala Phe Lys Arg Asn Leu Ser Leu Leu Lys Asp Ile Glu Ala Ala 55 Glu Lys Ser Leu Gln Thr Arg Ile His Pro Leu Pro Arg Pro Glu Val 70 Val Ser Leu Glu Thr Arg Tyr Trp Ala Ser Val Glu Glu Tyr Ile Pro 90 Lys Trp Glu Gln Phe Leu Leu Gly Arg Ala Pro Tyr Pro Phe Ala Val 100 105

Glu Asn Gln Asn Glu Ala Glu Asn Thr Ile Gln Asn Glu Ala Gln Arg

120 <210> 91 <211> 709 <212> DNA <213> Homo sapiens <400> 91 gteactteeg ceategtggt cateacttea ggeategeag ceategtgtt gteacgetae 60 ctccctagca ccccctgcg ctggacagtg tttagctcga gcgtggcctg tgctctcctt 120 tetetgacet gtgccetegg cetettggce tecategeca tgacetttge cacceaggge 180 aaggcactgc tggctgcctg cacttttggg agctctgaac tactggccct cgcacctgac 240 tgtccettcg accccacacg catttatage tecagectgt geetetgggg categeecta 300 gtgctctgcg tggcggagaa cgtgtttgct gtacgctgtg ctcagctcac ccaccagctg 360 ctggagctga ggccctggtg ggggaaaagc agccaccaca tgatgcggga gaacccagag 420 ctggtggagg gccgtgacct gctgagctgc accagctctg agcctctgac cctctgagag 480 atgatgteet geeeaggeee gatggeeact aggaceetge aageaactet getetgtgae 540 caggccagga ttcctggagc tggcctgaga gggctcaatg gaccctcggg gacccaagtg 600 gggctttcaa ccctctcccc caccaccag cccactgcac tgaaatgaga ctttattctg 660 <210> 92 <211> 105 <212> PRT <213> Homo sapiens <400> 92 Met Thr Phe Ala Thr Gln Gly Lys Ala Leu Leu Ala Ala Cys Thr Phe 10 . Gly Ser Ser Glu Leu Leu Ala Leu Ala Pro Asp Cys Pro Phe Asp Pro 20 25 Thr Arg Ile Tyr Ser Ser Ser Leu Cys Leu Trp Gly Ile Ala Leu Val Leu Cys Val Ala Glu Asn Val Phe Ala Val Arg Cys Ala Gln Leu Thr 55 50 His Gln Leu Leu Glu Leu Arg Pro Trp Trp Gly Lys Ser Ser His His 70 75 Met Met Arg Glu Asn Pro Glu Leu Val Glu Gly Arg Asp Leu Leu Ser 85 Cys Thr Ser Ser Glu Pro Leu Thr Leu 100 <210> 93 <211> 419 <212> DNA <213> Homo sapiens <400> 93 aggaaggaca ccaatgaatc agcttgggac ctctttaggc cttccccttt tcctccaccc 60 egatgeteet tagtgatget etgaggegtg gecaegatet eceteceagg tggtategee 120 cacctgaaaa aatcctgaga atttctccca tcttggcctc ttccagaaac cggccaggca 180

```
aggaaagagg ccggtcacca gaagccagca ggcgtggggt gtgatactct ctatagccac 240
   tacagggcgc gcgcaggtcg cggatctccc cagttgctaa tcccggctct gccactcaat 300
   cetateceta gttcccgage gegggteece egeettgeag tetecageeg tgeggggeeg 360
   ggagcaggec teeggeetee cagaetteta gagecegeeg ggeceatett tgtaeteat 419
   <210> 94
   <211> 93
   <212> PRT
<213> Homo sapiens
   <400> 94 .
   Glu Phe Leu Pro Ser Trp Pro Leu Pro Glu Thr Gly Gln Ala Arg Lys
                                       10
                    5
    1
                                                           15
   Glu Ala Gly His Gln Lys Pro Ala Gly Val Gly Cys Asp Thr Leu Tyr
                                   25
   Ser His Tyr Arg Ala Arg Ala Gly Arg Gly Ser Pro Gln Leu Leu Ile
                               40
           35
                                              45
   Pro Ala Leu Pro Leu Asn Pro Ile Pro Ser Ser Arg Ala Arg Val Pro
                           55
   Arg Leu Ala Val Ser Ser Arg Ala Gly Pro Gly Ala Gly Leu Arg Pro
   Pro Arg Leu Leu Glu Pro Ala Gly Pro Ile Phe Val Leu
                   85
   <210> 95
  <211> 220
   <212> DNA
   <213> Homo sapiens
   <220>
  <221> unsure
   <222> (37)
   <220>
   <221> unsure
  <222> (55)
   <220>/
   <221> unsure
   <222> (69)
   <220>
   <221> unsure
   <222> (86)
   <220>
   <221> unsure
  <222> (103)
   <220>
   <221> unsure
   <222> (155)
```

<220>

```
PCT/US99/31005
  WO 00/37630
 <221> unsure
 <222> (157)
 <220>
 <221> unsure
 <222> (167)
 <220>
 <221> unsure
 <222> (178)
 <220>
<221> unsure
 <222> (193)
 <400> 95
 tttgtttgcc atttattagc catgtgaaat tggccanatc aattcacctc cctgngcctc 60
 agtttcctna tttgtcaaat gggggnttat. aaacacctac ctngcagggt tgttgtgagg 120
 atttaatgcg ataatgtatg taaagcgcct tgcanantgc ctggcanaca gtaggcgntc 180
 aataaattta agnttccctt taaaaaaaaa aaaaaaaaaa
 <210> 96
 <211> 431
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> unsure
 <222> (29)
 <220>
 <221> unsure
 <222> (82)
 <220>
 <221> unsure
 <222> (106)
 <220>
 <221> unsure
 <222> (118)
 <220>
 <221> unsure
 <222> (167)..(168)
 <220>
 <221> unsure
 <222> (182)
. <220>
 <221> unsure
 <222> (190)
 <220>
 <221> unsure
 <222> (204)
```

<220> <221> unsure

```
<222> (214)
<400> 96
cacgaggggc agtgtttgct tttgccganc tggtgtccga cagctccctg ggtgtccggg 60
gtgggagaac tgttgacaga anctotoogg goodtoaggg gottanatoc cacttganto 120
gtaagcette ttgettttga taacacagta ttatttetet taetgtnnaa aaaaaaattt 180
tnttaccaan caagaatttt tttnggaaag aaanggacaa acctataaat taactcaacc 240
tatatetece ttgaaaatae ttteaggete caccaaaaeg tagaaetgaa ageatgtatt 300
ttggaagaaa gagatacatt ttgtatgctt tcttttcctt ttgtagattc ccagtttatt 360
ttctaagact gcaaagatca ctttgtcacc agccctggga cctgagacca agggggtgtc 420
ttgtgggcag t
<210> 97
<211> 46
<212> PRT
<213> Homo sapiens
<400> 97
Met Tyr Phe Gly Arg Lys Arg Tyr Ile Leu Tyr Ala Phe Phe Ser Phe
                                     10
Cys Arg Phe Pro Val Tyr Phe Leu Arg Leu Gln Arg Ser Leu Cys His
                                 25
Gln Pro Trp Asp Leu Arg Pro Arg Gly Cys Leu Val Gly Ser
                             40
<210> 98
<211> 341
<212> DNA
<213> Homo sapiens
<220>
<221> unsure
<222> (82)
<220>
<221> unsure
<222> (216)
<220>
<221> unsure
<222> (219)
<220>
<221> unsure
<222> (222)
<220>
<221> unsure
<222> (311)
<400> 98
tgtgtcttgg agctgactta ctaagtggaa tgagccgagg atttgaatat cagttctaac 60
cttgatagaa gaaccttggg tnacatgtgg ttcacattaa gaggatagaa tcctttggaa 120
tottatggca accaaatgtg gottgacgaa gtcgtggttt tattttttaa acaccggtgt 180
gtaaatttat tcaactaacg atgggaaatg tattanttnt gnacacagtg gactgaagtg 240
caatttgttg aaagggaaca agtcattgaa gagaaaaaaa aaagcccaat acttagagtc 300
```

ccaattttgt ntcatttgcc aaaaaaaaaa aaaaaaaaaa a

```
<210> 99
<211> 1491
<212> DNA
<213> Homo sapiens
<400> 99
ggacacctct tggagtccac ttggcatgat tacccgttga gccacatatt ggaaaaatga 60
ttetttttgg ageaetgtte tgetgettag acceagtaet cactattget getagtetea 120
aggaattggc aaaggatact agaagtgatc acttaacagt tgtgaatgcg tttgagggct 240
qqqaaqaqqc taggcgacgt ggtttcagat acgaaaagga ctattgctgg gaatattttc 300
tgtcttcaaa cacactgcag atgctgcata acatgaaagg acagtttgct gagcatcttc 360
ttggagctgg atttgtaagc agtagaaatc ctaaagatcc agaatctaat ataaattcag 420
ataatgagaa gataattaaa gctgtcatct jtgctggttt atatcccaaa gttgctaaaa 480
ttcgactaaa tttgggtaaa aaaagaaaaa tggtaaaagt ttacacaaaa accgatggcc 540
tggttgctgt tcatcctaaa tctgttaatg tggagcaaac agactttcac tacaactggc 600
ttatctatca cctaaagatg agaacaagca gtatatactt gtatgactgc acagaggttt 660
ecceatactg tetetigtti titiggaggig acatticeat ecagaaggat aacgateagg 720
aaactattgc tgtagatgag tggattgtat ttcagtctcc agcaagaatt gcccatcttg 780
ttaaggaatt aagaaaggaa ctagatattc ttctgcaaga gaagattgaa agtcctcatc 840
ctgtagactg gaatgacact aaatccagag actgtgcagt actgtcagct attatagact 900
tgatcaaaac acaggaaaag gcaactccca ggaactttcc gccacgattc caggatggat 960
attacagetg acagetttte aggggtggte tgaaaageca gtttgacage cattetteat 1020
cattgtttaa attttggctg gatgccaaac cctgggacat gaacaatttt catgtgtaag 1080
gtagaageet teagtaggta gtaaagaett aatgtgeatg aettgatgtt atatgtagag 1140
atatatatat atatatata ataccataaa agcaatatgt tototgatca tataccotgc 1200
tgtggtcatg cccactcttt gggagtatat tccctttata tatattgagt attgtaccac 1260
ttgagaaatt cctttgttct gttatacaaa attaatcttt ctgctcataa tgattgatga 1320
taccaccagt aaaaatagga tgtttacccc aaaacaagtg tcaattaaga atttgaacac 1380
aaccacattt tttaaaatga aacttctatc ggaagtaaat taatttgttg taataaagtc 1440
<210> 100
<211> 304
<212> PRT
<213> Homo sapiens
<400> 100
Met Ile Leu Phe Gly Ala Leu Phe Cys Cys Leu Asp Pro Val Leu Thr
                                  10
Ile Ala Ala Ser Leu Ser Phe Lys Asp Pro Phe Val Ile Pro Leu Gly
Lys Glu Lys Ile Ala Asp Ala Arg Arg Lys Glu Leu Ala Lys Asp Thr
                           40
Arg Ser Asp His Leu Thr Val Val Asn Ala Phe Glu Gly Trp Glu Glu
Ala Arg Arg Gly Phe Arg Tyr Glu Lys Asp Tyr Cys Trp Glu Tyr
                                      75
65
                   70
Phe Leu Ser Ser Asn Thr Leu Gln Met Leu His Asn Met Lys Gly Gln
Phe Ala Glu His Leu Leu Gly Ala Gly Phe Val Ser Ser Arg Asn Pro
           100
                              105
```

PCT/US99/31005

WO 00/37630 Lys Asp Pro Glu Ser Asn Ile Asn Ser Asp Asn Glu Lys Ile Ile Lys 120 Ala Val Ile Cys Ala Gly Leu Tyr Pro Lys Val Ala Lys Ile Arg Leu 135 Asn Leu Gly Lys Lys Arg Lys Met Val Lys Val Tyr Thr Lys Thr Asp 155 Gly Leu Val Ala Val His Pro Lys Ser Val Asn Val Glu Gln Thr Asp 165 170 Phe His Tyr Asn Trp Leu Ile Tyr His Leu Lys Met Arg Thr Ser Ser 185 Ile Tyr Leu Tyr Asp Cys Thr Glu Val Ser Pro Tyr Cys Leu Leu Phe 195 200 Phe Gly Gly Asp Ile Ser Ile Gln Lys Asp Asn Asp Gln Glu Thr Ile 215 Ala Val Asp Glu Trp Ile Val Phe Gln Ser Pro Ala Arg Ile Ala His Leu Val Lys Glu Leu Arg Lys Glu Leu Asp Ile Leu Leu Gln Glu Lys 245 Ile Glu Ser Pro His Pro Val Asp Trp Asn Asp Thr Lys Ser Arg Asp 260 265 Cys Ala Val Leu Ser Ala Ile Ile Asp Leu Ile Lys Thr Gln Glu Lys 275 280 Ala Thr Pro Arg Asn Phe Pro Pro Arg Phe Gln Asp Gly Tyr Tyr Ser 295 <210> 101 <211> 220 <212> DNA <213> Homo sapiens <220>

<221> unsure

<222> (139)

<220>

<221> unsure

<222> (208)..(209)

<400> 101

cagaagetgt accacaagaa gatetteegg actgecatge tgtteeagtt tgtgaaegtg 60 ctgctccagg tcctggtcca caagtcccat gatcttctgc aggaggagat tggcatcgcc 120 atctacaaca tggcctcant cgactttgat ggcttctttg ccgccttcct cccagagttc 180 ctgaccagct gtgatggtgt ggatgccnnc cagaaaagtt

<210> 102

<211> 61

<212> PRT

<213> Homo sapiens

```
<220>
<221> UNSURE
<222> (35)
<220>
<221> UNSURE
<222> (58)
<400> 102
Met Leu Phe Gln Phe Val Asn Val Leu Leu Gln Val Leu Val His Lys
                 5
                                   10
Ser His Asp Leu Leu Gln Glu Glu Ile Gly Ile Ala Ile Tyr Asn Met
Ala Ser Xaa Asp Phe Asp Gly Phe Phe Ala Ala Phe Leu Pro Glu Phe
       35 40
Leu Thr Ser Cys Asp Gly Val Asp Ala Xaa Gln Lys Ser
                       55
                                          60
<210> 103
<211> 251
<212> DNA
<213> Homo sapiens
<220>
<221> unsure
<222> (17)
<220>
<221> unsure
<222> (72)
<220>
<221> unsure
<222> (77)
<220>
<221> unsure
<222> (100)
<220>
<221> unsure
<222> (108)
<220>
<221> unsure
<222> (132)
<220>
<221> unsure
<222> (134)
<220>
<221> unsure '
```

<222> (171)

```
PCT/US99/31005
 WO 00/37630
<220>
<221> unsure
<222> (179)
<220>
<221> unsure
<222> (227)
<400> 103
acgacagtgc caccttntca ccattccagc caaggagaga tgtgacgttg gaactgcttt 60
ggcaattttg tnaagcntcc cccgccccaa ttgccttgan atttttgntt tttgtcagag 120
atttgcaaag antnaagttt ttgttgtttt ttcatcattc cattgtgata ntaagaaant 180
aagaagctta atgaaaagaa ataaaatgcc tatgttgttg ttttagnaaa aaaaaaaaaa 240
aaaaaaaaa a
<210> 104
<211> 422
<212> DNA
<213> Homo sapiens
<220>
<221> unsure
<222> (9)
<220>
<221> unsure
<222> (11)
<220>
<221> unsure
<222> (355)
<400> 104
gaatteggna ngaggtetga ekggaettte tattaretea aeteeaceag etgteagtag 60
tgttctcagt acaggtgtac caacagtacc gttattgcca ccacaagtaa accagtccct 120
cacttctgtg ccaccaatga atccagctac tacattacca ggtctgatgc ctttaccagc 180
aggactgocc aacetececa aceteaacet caacetecca geaceacaca teatgecagg 240
ggttggctta ccagaacttg taaacccagg tctgccacct cttccttcca tgcctccccg 300
aaacttacct gggcattgca cetetteece etggecatec gagtteetee egttnattte 360
ccttgggttt ccagaggagg ttttttttgc aggcaaggtt cagggagagt tggtggtttt 420
<210> 105
<211> 140
<212> PRT
<213> Homo sapiens
<220>
<221> UNSURE
<222> (3)..(4)
<220>
<221> UNSURE
<222> (12)
<220>
<221> UNSURE
<222> (118)
<400> 105
```

```
Asn Ser Xaa Xaa Gly Leu Thr Gly Leu Ser Ile Xaa Ser Thr Pro Pro
                                      10
 Ala Val Ser Ser Val Leu Ser Thr Gly Val Pro Thr Val Pro Leu Leu
                                  25
 Pro Pro Gln Val Asn Gln Ser Leu Thr Ser Val Pro Pro Met Asn Pro
Ala Thr Thr Leu Pro Gly Leu Met Pro Leu Pro Ala Gly Leu Pro Asn
                         55
Leu Pro Asn Leu Asn Leu Asn Leu Pro Ala Pro His Ile Met Pro Gly
                      70
 Val Gly Leu Pro Glu Leu Val Asn Pro Gly Leu Pro Pro Leu Pro Ser
Met Pro Pro Arg Asn Leu Pro Gly His Cys Thr Ser Ser Pro Trp Pro
                                105
 Ser Glu Phe Leu Pro Xaa Ile Ser Leu Gly Phe Pro Glu Glu Val Phe
                            120
                                         125
 Phe Ala Gly Lys Val Gln Gly Glu Leu Val Val Phe
                        135
 <210> 106
 <211> 328
 <212> DNA
 <213> Homo sapiens
<220>
 <221> unsure
 <222> (76)
<400> 106
caggttgagt ggggctcaca cgctagggtg agatgtcaga aagcgcttgt attttaaaca 60
accaaaaaga attgtngggg tggcttgctg ccaggcttgc actgccgttc ctgggggtgt 120
gcatcttcgg gaaaggtggt ggcggggcgt ccactaggtt tcctgtcccc tgctgctcct 180
teegtaagaa aatgaaatat tetatgeeta ataeteacae geaacattte tigtaetitig 240
taagtcgttt gcgagaatgc agaccacctc actaaactgt aaacggtaaa gagattttta 300
cttttggtca aaaaaaaaa aaaaaaaa
<210> 107
<211> 896
<212> DNA
<213> Homo sapiens
<400> 107
cacgaggegg tggactgcaa ggacccagat gatgtggtac cagttggcca aagaagagcc 60
tggtgttggt gcatgtgctt tggactagca tttatgcttg caggtgttat tctaggagga 120
gcatacttgt acaaatattt tgcacttcaa ccagatgacg tgtactactg tggaataaag 180
tacatcaaag atgatgtcat citaaatgag ccctctgcag atgccccagc tgctctctac 240
cagacaattg aagaaaatat taaaatcttt gaagaagaag aagttgaatt tatcagtgtg 300
cctgtcccag agtttgcaga tagtgatcct gccaacattg ttcatgactt taacaagaaa 360
cttacagect atttagatet taacetggat aagtgetatg tgatecetet gaacaettee 420
attgttatgc cacccagaaa cctactggag ttacttatta acatcaaggc tggaacctat 480
ttgcctcagt cctatctgat tcatgagcac atggttatta ctgatcgcat tgaaaacatt 540
```

gateacetgg gtttetttat ttategacig tgteatgaca aggaaaceta caaacegeaa 600 cgcagagaaa ctattaaagg tattcagaaa cgtgaagcca gcaattgttt cgcaattcgg 660 cattttgaaa acaaatttgc cgtggaaact ttaatttgtt cttgaacagt caagaaaaac 720 attattgagg aaaattaata tcacagcata accccacct ttacattttg tgcagtgatt 780 attitttaaa gictictiic atgiaagtag caaacagggc titactaici titcatcica 840 <210> 108 <211> 210 <212> PRT <213> Homo sapiens <400> 108 Met Cys Phe Gly Leu Ala Phe Met Leu Ala Gly Val Ile Leu Gly Gly 10 Ala Tyr Leu Tyr Lys Tyr Phe Ala Leu Gln Pro Asp Asp Val Tyr Tyr 25 Cys Gly Ile Lys Tyr Ile Lys Asp Asp Val Ile Leu Asn Glu Pro Ser 40 Ala Asp Ala Pro Ala Ala Leu Tyr Gln Thr Ile Glu Glu Asn Ile Lys Ile Phe Glu Glu Glu Val Glu Phe Ile Ser Val Pro Val Pro Glu 70 Phe Ala Asp Ser Asp Pro Ala Asn Ile Val His Asp Phe Asn Lys Lys 85 90 Leu Thr Ala Tyr Leu Asp Leu Asn Leu Asp Lys Cys Tyr Val Ile Pro 105 Leu Asn Thr Ser Ile Val Met Pro Pro Arg Asn Leu Leu Glu Leu Leu 115 120 Ile Asn Ile Lys Ala Gly Thr Tyr Leu Pro Gln Ser Tyr Leu Ile His 135 Glu His Met Val Ile Thr Asp Arg Ile Glu Asn Ile Asp His Leu Gly . 150 155 Phe Phe Ile Tyr Arg Leu Cys His Asp Lys Glu Thr Tyr Lys Leu Gln 165 170 Arg Arg Glu Thr Ile Lys Gly Ile Gln Lys Arg Glu Ala Ser Asn Cys 185 Phe Ala Ile Arg His Phe Glu Asn Lys Phe Ala Val Glu Thr Leu Ile 200 Cys Ser 210 <210> 109

<210> 109 <211> 268 <212> DNA

<213> Homo sapiens

```
<400> 109
gtttgacctg gctggaataa cgtgtgggca cttccttgaa ccttcttgga ccttctttgg 60
tgcaaccctg attgggaaag caatcattaa aatgcatatc cagaaaatat ttgttatagt 120
aactttcagc aagcacatcg tggagcagat ggtgactttc attggtgctg tccccggcat 180
aggtccgtct ctgcagaagc cttttcaaga gtacctggag gcgcagcggc agaagcttca 240
tcacagaagt gaagegggca cacegeag
<210> 110
<211> 59
<212> PRT
<213> Homo sapiens
<400> 110
Met His Ile Gln Lys Ile Phe Val Ile Val Thr Phe Ser Lys His Ile
                                     10
Val Glu Gln Met Val Thr Phe Ile Gly Ala Val Pro Gly Ile Gly Pro
            20
                                25
Ser Leu Gln Lys Pro Phe Gln Glu Tyr Leu Glu Ala Gln Arg Gln Lys
Leu His His Arg Ser Glu Ala Gly Thr Pro Gln
    50
<210> 111
<211> 138
<212> DNA
<213> Homo sapiens
<220>
<221> unsure
<222> (33)
<220>
<221> unsure
<222> (44)
<400> 111
gagacagtat aaggaaaatc tggttggtgt ctnacaagtg agcngacacc atttttatt 60
ctgtgtattt agaatgaagt cttgaaaaaa acttaaaaaa gacaacttta atcattccaa 120
aaaaaaaaa aaaaaaaa
<210> 112
<211> 415
<212> DNA
<213> Homo sapiens
<220>
<221> unsure
<222> (211)
<220>
<221> unsure
<222> (225)
<220>
<221> unsure
```

### WO 00/37630

# PCT/US99/31005

<222> (234)

<220>

<221> unsure

<222> (238)

<220>

<221> unsure

<222> (243)

<220>

<221> unsure

<222> (251)

<220>

<221> unsure

<222> (255)

<220>

<221> unsure

<222> (262)

<220>

<221> unsure

<222> (269)

<220>

<221> unsure

<222> (274)

<220>

<221> unsure

<222> (285)

<220>

<221> unsure

<222> (289)

<220>

<221> unsure

<222> (298)

<220>

<221> unsure

<222> (300)

<220>

<221> unsure

<222> (320)

<220>

<221> unsure

<222> (323)

<220>

<221> unsure

<222> (337)

<220>

<221> unsure

```
<222> (350)
<220>
<221> unsure
<222> (353)
<220>
<221> unsure
<222> (355)
<220>
<221> unsure
<222> (378)
<220>
<221> unsure
<222> (382)
<220>
<221> unsure
<222> (393)..(394).
<220>
<221> unsure
<222> (403)
<22Ö>
<221> unsure
<222> (405)
<220>
<221> unsure
<222> (413)
<400> 112
aacagagaaa gaaaccaccc aagagtatat cagaatcggg atttccgagg tcacaacaga 60
ggctatagaa ggccctatta tttccgtggg cgtaacagag gcttttatcc atggggccaa 120
tataaccgag gaggctatgg aaactaccgc tcaaattggc agaattaccg gcaagcatac 180
agtectegte gaggeegtte aagateeegg neeceaaaaa aaagnteeee teeneeangg 240
tenagaacce nteenaaaac enetaatant tetneteeta acegnteang gececeenen 300
ccccccttc ctcccccan ccntacccaa tttaatnctc ctaacccan ttntncaaag 360
aaaaaaaatt cccctccnaa gnatacccgg ccnnctcagg ctncngggaa tancc
<210> 113
<211> 92
<212> PRT
<213> Homo sapiens
<220>
<221> UNSURE
<222> (30)
<220>
<221> UNSURE
<222> (33)..(34)
<220>
<221> UNSURE
<222> (36)
```

```
<220>
<221> UNSURE
<222> (39)..(40)
<220>
<221> UNSURE
<222> (45)
<220>
<221> UNSURE
<222> (50)..(51)
<220>
<221> UNSURE
<222> (55)
<220>
<221> UNSURE
<222> (62)..(63)
<220>
<221> UNSURE -
<222> (67)
<220>
<221> UNSURE
<222> (72)..(73)
<220>
<221> UNSURE
<222> (81)..(82)
<220>
<221> UNSURE
<222> (86)
<220>
<221> UNSURE
<222> (90)
<400> 113
Met Glu Thr Thr Ala Gln Ile Gly Arg Ile Thr Gly Lys His Thr Val
                                    10
Leu Val Glu Ala Val Gln Asp Pro Gly Pro Gln Lys Lys Xaa Pro Leu
                                25
            20
Xaa Xaa Gly Xaa Glu Pro Xaa Xaa Lys Pro Leu Ile Xaa Leu Leu Leu
                           40
Thr Xaa Xaa Gly Pro Pro Xaa Pro Pro Phe Leu Pro Pro Xaa Xaa Pro
                         55
Asn Leu Xaa Leu Leu Thr Pro Xaa Xaa Gln Arg Lys Lys Ile Pro Leu
65
                     70
                                         75
Xaa Xaa Ile Pro Gly Xaa Leu Arg Leu Xaa Gly Ile
```

90

85

# WO 00/37630

### PCT/US99/31005

- <210> 114
- <211> 268
- <212> DNA
- <213> Homo sapiens
- <220>
- <221> unsure
- <222> (37)
- <220>
- <221> unsure
- <222> (71)
- <220>
- <221> unsure
- <222> (73)
- <220>
- <221> unsure
- <222> (88)
- <220>
- <221> unsure
- <222> (99)
- <220>
- <221> unsure
- <222> (103)
- <220>
- <221> unsure
- <222> (106)
- <220>
- <221> unsure
- <222> (122)
- <220>
- <221> unsure
- <222> (127)
- <220>
- <221> unsure
- <222> (132)
- <220>
- <221> unsure
- <222> (134)
- <220>
- <221> unsure
- <222> (142)
- <220>
- <221> unsure
- <222> (146)
- <220>
- <221> unsure
- <222> (151)

```
<220>
<221> unsure
<222> (158)
<220>
<221> unsure
<222> (165)
<220>
<221> unsure
<222> (168)
<220>
<221> unsure
<222> (179)
<220>
<221> unsure
<222> (184)
<220>
<221> unsure
<222> (194)
<220>
<221> unsure
<222> (223)
<220>
<221> unsure
<222> (232)
<220>
<221> unsure
<222> (240)
<220>
<221> unsure
<222> (248)
<220>
<221> unsure
<222> (250)
<400> 114
aatttgccga gtggtgccgg gtatcagttt gggaaanacc aaggtcagtt tgaccatggt 60
tttgggtccc ngngtccatc caaaaagngc cctgtgggna agngtncacc atccaatggg 120
tncaaanatg gntnatttca gnaggnggag ngtgctgntt caggnggngc agcctatana 180
aagnggtatt tagnagagca gaagacagag gatgggaaag atnagggaca gnaacaaacn 240
                                                                   268
aataccgntn aaaaaaaaa aaaaaaaa
<210> 115
<211> 323
<212> DNA
<213> Homo sapiens
<220>
<221> unsure
```

<222> (245)..(247)

```
<220>
<221> unsure
<222> (275)
<400> 115
acagageete taeetggeag gaaacaagte egggataett tggeageaat eteagaagtt 60
ctttatgttg atttgctaga aggggataca gaatgccatg ctagatttaa aactcctgag 120
gatgctcaag cagtaataaa tgcctataca gaaattaaca agaaacactg ctggaaactc 180
gagatccttt ctggtgatca cgaacaaagg tattggcaga agattttggt tgatagaaag 240
gcaannntta atcagcctcg ggaaaagaaa agagnggtga aaagttaatc accagagctg 300
aaaagattag actggcaaag act
<210> 116
<211> 95
<212> PŘT
<213> Homo sapiens
<220>
<221> UNSURE
<222> (82)..(83)
<220>
<221> UNSURE
<222> (92)
<400> 116
Thr Glu Pro Leu Pro Gly Arg Lys Gln Val Arg Asp Thr Leu Ala Ala
                                     10
Ile Ser Glu Val Leu Tyr Val Asp Leu Leu Glu Gly Asp Thr Glu Cys
His Ala Arg Phe Lys Thr Pro Glu Asp Ala Gln Ala Val Ile Asn Ala
Tyr Thr Glu Ile Asn Lys Lys His Cys Trp Lys Leu Glu Ile Leu Ser
                         55
    50
Gly Asp His Glu Gln Arg Tyr Trp Gln Lys Ile Leu Val Asp Arg Lys
Ala Xaa Xaa Asn Gln Pro Arg Glu Lys Lys Arg Xaa Val Lys Ser
                 85
                                     90
<210> 117
<211> 190
<212> DNA
<213> Homo sapiens
<220>
<221> unsure
<222> (15)
<220>
<221> unsure
<222> (18)
```

<220>

```
<222> (31)
<220>
<221> unsure
<222> (40)
<220>
<221> unsure
<222> (58)
<220>
<221> unsure
<222> (62)
<220>
<221> unsure
<222> (65)
<220>
<221> unsure
<222> (70)
<220>
<221> unsure
<222> (72)
<220>
<221> unsure
<222> (74)
<220>
<221> unsure
<222> (80)
<220>
<221> unsure
<222> (93)
<220>
<221> unsure
<222> (120)
<220>
<221> unsure
<222> (124)
<220>
<221> unsure
<222> (133)
<220>
<221> unsure
<222> (149)
<220>
<221> unsure
```

<222> (161)

<400> 117

<221> unsure

```
tttttaatta aaagnaanat ttttgttcct naaattgtan ataagaattt tttttagnga 60
cnaanatgan gnanaccacn attititita aanattitat tigitigaaat tattitagan 120
gtcngtgtca ggngatttag taaataaang tgttttggac ntttaaaaaa aaaaaaaaaa 180
aaaaaaaaa
<210> 118
<211> 294
<212> DNA
<213> Homo sapiens
<400> 118
ggcatctgca acctgctcct ttacttcgcc ttctacatca tcatgaagct ccggagtggg 60
gagaggatca ageteateee cetgetetge ategtttgea ceteegtggt etggggette 120
gegetettet tettetteca gggaeteage acetggeaga aaacecetge agagtegagg 180
gagcacaacc gggactgcat cctcctcgac ttctttgacg accacgacat ctggcacttc 240
ctctcctcca tcgccatgtt tcgggtcctt cctggtgttt gctgacactg gatg
<210> 119
<211> 80
<212> PRT
<213> Homo sapiens
<400> 119
Met Lys Leu Arg Ser Gly Glu Arg Ile Lys Leu Ile Pro Leu Leu Cys
                                    10
Ile Val Cys Thr Ser Val Val Trp Gly Phe Ala Leu Phe Phe Phe Phe
Gln Gly Leu Ser Thr Trp Gln Lys Thr Pro Ala Glu Ser Arg Glu His
                            40
Asn Arg Asp Cys Ile Leu Leu Asp Phe Phe Asp Asp His Asp Ile Trp
     50
                        55
                                            60
His Phe Leu Ser Ser Ile Ala Met Phe Arg Val Leu Pro Gly Val Cys
 65
                    70
                                        75
<210> 120
<211> 230
<212> DNA
<213> Homo sapiens
<220>
<221> unsure
<222> (38)
<220>
<221> unsure
<222> (46)
<400> 120
accecagatg ctgaggatgg gggagctcag gcggggcntc tgcttngggg atgggaatgt 60
gtttttctcc caaacttgtt tttatagctc tgcttgaagg gctgggagat gaggtgggtc 120
tggatctttt ctcagagcgt ctccatgcta tggttgcatt tccgttttct atgaatgaat 180
<210> 121
```

<211> 495

```
<212> DNA
<213> Homo sapiens
<220>
<221> unsure
<222> (429)
<220>
<221> unsure
<222> (467)
<400> 121.
gacctgcctt cctgctcttc taggtagtca cacttcacta aagtgtcatc caccagtgtg 60
ttgaatccga agaatgacaa ttttctacca ctggtgtaaa aaacaaacat ttgaagaccc 120
ttgtgcattg tgtgtcacaa agctaaatac atggaaatcg ttaatatcgc tgatattaag 180
taatttcccc actctgagtg aatactttga tgattgccaa cagtggctaa taaaatgacg 240
getaceacae teatgggtea etggggetge geagggetet ttgaggtggg tggettettt 300
tggaaagtac tatgaacgtc tcgaagcagt attctagtga taagaattct taacatagcc 360
aagegeecca egittgitee ecaegittgi teeeettite tgittgaaaa accigitetg 420
gtageteene aagagagatg atactgaett titaaattit titacaanagt etgtatteet 480
gatatgccta tattt
<210> 122
<211> 41
<212> PRT
<213> Homo sapiens
<400> 122
Thr Ser Arg Ser Ser Ile Leu Val Ile Arg Ile Leu Asn Ile Ala Lys
                                     10
Arg Pro Thr Phe Val Pro His Val Cys Ser Pro Phe Leu Phe Glu Lys
Pro Val Leu Val Ala Pro Gln Glu Arg
         35
                             40
<210> 123
<211> 18
<212> DNA
<213> Homo sapiens
<400> 123
                                                                   18
gaaaaaaaa aaaaaaaa
<210> 124
<211> 285
<212> DNA
<213> Homo sapiens
<220>
<221> unsure
<222> (135)
```

<220>
<221> unsure
<222> (234)

<400> 124

```
cacgaagggt ttcaaggtct gtcttagttc tcattctcaa gattgtttcc agttgcaagt 60
tagaggcaag ccagctagct gcccagcctt aactctgttc agtgccctgt tactaacatt 120
ttttaacaga ttggnttcta catgtttaaa gtatccagcg ttggatttta cctcttgcta 180
gttccatttg tccctggtgc tgcttttaaa ggtatagggc cctgtgaagt ggantatgta 240
cgcagttggc ctggtgatgt atctgtgcct gttttatctt ctccc
<210> 125
<211> 48
<212> PRT
<213> Homo sapiens
<220>
<221> UNSURE
<222> (31)
<400> 125
Met Phe Lys Val Ser Ser Val Gly Phe Tyr Leu Leu Val Pro Phe
                                     10
Val Pro Gly Ala Ala Phe Lys Gly Ile Gly Pro Cys Glu Val Xaa Tyr
             20
                                 25
Val Arg Ser Trp Pro Gly Asp Val Ser Val Pro Val Leu Ser Ser Pro
                             40
<210> 126
<211> 350
<212> DNA
<213> Homo sapiens
<220>
<221> unsure
<222> (5)
<220>
<221> unsure
<222> (215)
<400> 126
ttccntatgt aagatgtcat actgcagatt taaaatatag actatcaata aaatgcatga 60
agtgatcatt tgtgcttgat catctctcct tgggtttttc tttaaaaagg ggaatctgct 120
atadaggttc tgttgcttca aaccaatgtc aaatagactt gatttttaga gtcatggaat 180
tacagtgcaa ccttgatttt tattcccctc actgntatga gtgtgggcag gtactggttt 240
atatgttata acttccgttt tatctgtgtt gtgtagttga atggcttaat cgttgagtgg 300
taaaataaaa gattatatto caatacaagg aaaaaaaaaa aaaaaaaaaa
<210> 127
<211> 517
<212> DNA
<213> Homo sapiens
<220>
<221> unsure
<222> (63)
<400> 127
cacgaggcct cgtgccaaca ggaaagttgc tttgttttgc ttcgagatgg ctgcggggat 60
gtntttggaa cattatctgg acagtattga aaacctcccg tttgaattac agagaaactt 120
tragctcatg agggacctag accaaaggac agaggacctg aaggctgaaa ttgacaagtt 180
```

```
ggccactgaa tatatgagta gcgcccgcag cctgagctcc gaggagaagc tggcccttct 240
cagacagatc caggaggcct atggcaagtg caaggaattt ggtgacgaca aggtgcagct 300
ggccatgcag acctatgaga tggtagacaa acacattcgg cggctggaca cagacctggc 360
ccgttttgag gctgatctga aggagaaaca gatcgagtcc agtgactatg acagctcttc 420
tagcaaaggc aaaaagagcc ggacccaaaa ggagaaaaaa gctgccagag cccgttccaa 480
agggaaaaac tcagatgaag aagcccccaa ggctgcc
<210> 128
<211> 157
<212> PRT
<213> Homo sapiens
<220>
<221> UNSURE
<222> (6)
<400> 128
Met Ala Ala Gly Met Xaa Leu Glu His Tyr Leu Asp Ser Ile Glu Asn
                                    10
                 5
Leu Pro Phe Glu Leu Gln Arg Asn Phe Gln Leu Met Arg Asp Leu Asp
                                 25
Gln Arg Thr Glu Asp Leu Lys Ala Glu Ile Asp Lys Leu Ala Thr Glu
Tyr Met Ser Ser Ala Arg Ser Leu Ser Ser Glu Glu Lys Leu Ala Leu
                        55
Leu Arg Gln Ile Gln Glu Ala Tyr Gly Lys Cys Lys Glu Phe Gly Asp
                     70
Asp Lys Val Gln Leu Ala Met Gln Thr Tyr Glu Met Val Asp Lys His
                 85
                                    90
Ile Arg Arg Leu Asp Thr Asp Leu Ala Arg Phe Glu Ala Asp Leu Lys
Glu Lys Gln Ile Glu Ser Ser Asp Tyr Asp Ser Ser Ser Ser Lys Gly
    115
                          120
Lys Lys Ser Arg Thr Gln Lys Glu Lys Lys Ala Ala Arg Ala Arg Ser
                       135
                                           140
Lys Gly Lys Asn Ser Asp Glu Glu Ala Pro Lys Ala Ala
                   150
<210> 129
<211> 246
<212> DNA
<213> Homo sapiens
<220>
<221> unsure
<222> (24)
<220>
<221> unsure
<222> (27)..(28)
```

```
<220>
<221> unsure
<222> (30)
<220>
<221> unsure
<222> (33)
<220>
<221> unsure
<222> (87)
<220>
<221> unsure
<222> (122)
<400> 129
teetgtggtg agggetaggt gtgntennen etnttattet ceatteeett eetgettttt 60
tcatggtggg ggatccacca ggtcatntag gctctggccc tagttgaagg ggcacccctt 120
cntctgtgcc aagaggattc atcctgggag agggggcaag gtggaatgca gataactcac 180
atgtaaaagg aacttgggta ggtaaataaa agctatacat gttgaaaaaa aaaaaaaaa 240
aaaaaa
<210> 130
<211> 694
<212> DNA
<213> Homo sapiens
<220>
<221> unsure
<222> (17)
<220>
<221> unsure
<222> (62)
<220>
<221> unsure
<222> (363)
<220>
<221> unsure
<222> (368)
<220>
<221> unsure
<222> (413)
<220>
<221> unsure
<222> (416)
<220>
<221> unsure
<222> (424)
```

<220>
<221> unsure
<222> (465)

```
<220>
<221> unsure
<222> (473)
<220>
<221> unsure
<222> (495)
<220>
<221> unsure
<222> (499)
<220>
<221> unsure
<222> (522)
<220>
<221> unsure
<222> (548)
<220>
<221> unsure
<222> (566)
<220>
<221> unsure
<222> (584)
<220>
<221> unsure
<222> (620)
<220>
<221> unsure
<222> (651)..(652)
<220>
<221> unsure
<222> (667)
<220>
<221> unsure
<222> (679)
<400> 130
aagettggea egagggneaa acetetatgg atatataaag ggaagettga ggaggaattt 60
cncagttaca gtgcagaagc acaagcaaaa gaattaacca gctcttcagt caagcaaatc 120
ctctactcac catgettect cetgecatte atttetatet cetteceett geatgeatee 180
taatgaaaag ctgtttggct tttaaaaatg atgccacaga aatcctttat tcacatgtgg 240
ttaaacctgt tccagcacac cccagcagca acagcacgtt gaatcaagcc agaaatggtt 300
gcaggcattt cagtaacact ggactggatc ggaacactcg ggttcaagtg ggttgccggg 360
aankgcgntc ccaccaaata catctctgat ggccagtgca ccagcatcag ccntangaag 420
gagntggtgt gtgctggcga gtgacttgcc cctgccagtg ctccntaatt ggnttggagg 480
aggctgtgga acaangtant ggagcaggag gagctcccag gngtggcggt gtgtcaatga 540
caaaaccngt acccagagaa tccagntgca gttccaagat ggcngcacac gcacgtacaa 600
aatcacagta gtcggtgccn gcaagtgcaa gaggtacacc cggcagcaca nngagtccag 660
tcacganttt gagagcatnt cacgtgccaa gcca
```

<210> 131

```
WO 00/37630 PCT/US99/31005
```

```
<211> 102
<212> PRT
<213> Homo sapiens
<220>
<221> UNSURE
<222> (9)..(10)
<220>
<221> UNSURE
<222> (12)
<220>
<221> UNSURE
<222> (26)
<220>
<221> UNSURE
<222> (29)
<220>
<221> UNSURE
<222> (36)..(37)
<220>
<221> UNSURE
<222> (45)
<220>
<221> UNSURE
<222> (54)
<220>
<221> UNSURE
<222> (60)
<220>
<221> UNSURE
<222> (66)
<220>
<221> UNSURE
<222> (78).
<220>
<221> UNSURE
<222> (88)
<220>
<221> UNSURE
<222> (93)
<220>
<221> UNSURE
<222> (97)
<400> 131
Met Ala Ser Ala Pro Ala Ser Ala Xaa Xaa Arg Xaa Trp Cys Val Leu
                                                         15
```

Ala Ser Asp Leu Pro Leu Pro Val Leu Xaa Asn Trp Xaa Gly Gly 20 25 Cys Gly Thr Xaa Xaa Trp Ser Arg Arg Ser Ser Gln Xaa Trp Arg Cys 40 Val Asn Asp Lys Thr Xaa Thr Gln Arg Ile Gln Xaa Gln Phe Gln Asp 55 Gly Xaa Thr Arg Thr Tyr Lys Ile Thr Val Val Gly Ala Xaa Lys Cys 75 70 Lys Arg Tyr Thr Arg Gln His Xaa Glu Ser Ser His Xaa Phe Glu Ser 90 Xaa Ser Arg Ala Lys Pro 100 <210> 132 <211> 243 <212> DNA <213> Homo sapiens <220> <221> unsure <222> (53) <400> 132 atatgaaata catgttgtag atatgtaaaa tgaatatttt agtctccctt atnacatata 60 tgttcatggt gaactttatc aatagtatgg atctttttaa atcaataaga tgctttgtaa 120 agttgaaata agtaatactt tottgtttaa totgtgcaat cagaaggtgt ottgacetto 180 aattcaattg gtttctttta acaaaaataa acactgctaa aagttaaaaa aaaaaaaaa 240 aaa <210> 133 <211> 1187 <212> DNA <213> Homo sapiens <400> 133 tgtcagagtt ggtctgttac tcggtggtgg cggagtctac ggaagccgtt ttcgcttcac 60 ttttcctggc tgtagagcgc tttccccctg gcgggtgaga gtgcagagac gaaggtgcga 120 gatgageact atgttegegg acaeteteet categttttt atetetgtgt geaeggetet 180 gctcgcagag ggcataacct gggtcctggt ttacaggaca gacaagtaca agagactgaa 240 ggcagaagtg gaaaaacaga gtaaaaaatt ggaaaagaag aaggaaacaa taacagagtc 300 agctggtcga caacagaaaa agaaaataga gagacaagaa gagaaactga agaataacaa 360 cagagateta teaatggtte gaatgaaate catgtttget attggetttt gttttactge 420 cctaatggga atgttcaatt ccatatttga tggtagagtg gtggcaaagc ttccttttac 480 ccctctttct tacatccaag gactgtctca tcgaaatctg ctgggagatg acaccacaga 540 ctgttccttc attttcctgt atattctctg tactatgtcg attcgacaga acattcagaa 600 gattetegge ettgeeeett cacgageege caccaageag geaggtggat ttettggeee 660 accacctcct totgggaagt totottgaac toaagaactc tttattttct atcattcttt 720 ctagacacac acacatcaga ctggcaactg ttttgtagca agagccatag gtagccttac 780 tacttgggcc tctttctagt tttgaattat ttctaagcct tttgggtatg attagagtga 840 aaatggcagc cagcaaactt gatagtgctt ttggtcctag atgattttta tcaaataagt 900 ggattgatta gttaagttca ggtaatgttt atgtaatgaa aaacaaatag catccttctt 960 gtttcattta cataagtatt ttctgtggga ccgactctca aggcactgtg tatgccctgc 1020 aagttggctg totatgagca tttagagatt tagaagaaaa atttagtttg tttaaccctt 1080 gtaactgttt gttttgttgt tgttttttt tcaagccaaa tacatgacat aagatcaata 1140

<210> 134 <211> 188 <212> PRT <213> Homo sapiens <400> 134 Met Ser Thr Met Phe Ala Asp Thr Leu Leu Ile Val Phe Ile Ser Val Cys Thr Ala Leu Leu Ala Glu Gly Ile Thr Trp Val Leu Val Tyr Arg Thr Asp Lys Tyr Lys Arg Leu Lys Ala Glu Val Glu Lys Gln Ser Lys 40 Lys Leu Glu Lys Lys Lys Glu Thr Ile Thr Glu Ser Ala Gly Arg Gln 55 Gln Lys Lys Lys Ile Glu Arg Gln Glu Glu Lys Leu Lys Asn Asn Asn 70 Arg Asp Leu Ser Met Val Arg Met Lys Ser Met Phe Ala Ile Gly Phe Cys Phe Thr Ala Leu Met Gly Met Phe Asn Ser Ile Phe Asp Gly Arg 105 Val Val Ala Lys Leu Pro Phe Thr Pro Leu Ser Tyr Ile Gln Gly Leu 120 Ser His Arg Asn Leu Leu Gly Asp Asp Thr Thr Asp Cys Ser Phe Ile 135 Phe Leu Tyr Ile Leu Cys Thr Met Ser Ile Arg Gln Asn Ile Gln Lys 155 150 Ile Leu Gly Leu Ala Pro Ser Arg Ala Ala Thr Lys Gln Ala Gly Gly 165 170 Phe Leu Gly Pro Pro Pro Pro Ser Gly Lys Phe Ser 180 185 <210> 135 <211> 1300 <212> DNA <213> Homo sapiens <400> 135 tactgactcg aggccaagaa ttcggcacga ggcaattttt aatttttgtt aatatcaaca 60 gcaaaagcct agtgcattgg gagatgtgca acctccctga aaatcttttc tgtttctgga 120

gtacttcagg ggtggcctct ggcccagag cetttgccac agtgctcca ccagcccca 180 cctcatccgt ctgtttgcag agcctcatct acaggtcccc acgctgcctt ctttactcac 240 tctgcgcttg gccgtttgt tatttggctt agtctacatt gggcggaagt ctgtgtgcac 300 agagtgggtg ttccttcgag ccccttccac tcagagggcc acacccagcg atgccagtga 360 aggtggcaca gcctctctc agtttccct gactgtgatc tcactggggt agaattcccc 420 tgagagaatt ccctcactca cggctcctt tgccagagtc agttcaatca ggtctgatgt 480 gagcaattta cacacttgtc tcagaaagtc ccccagggtt tgtagaggac tgcaggggg 540

```
catcogotgo agactoagoo tttototgoa gooatootgo agtgggggtg agogggoaca 600
ggctgagaac tgctcttggg tggtggaagc aggtgtcacg gtgcaagtct ccccctgcac 660
coetcecca gettgageeg tgtcacccc ctetecetee ageatgggee tgtgteteag 720
getetetgga aggtggeeet geeeeggaee etettgeagg tgteetggtt tgaettggaa 780
ctagatggcc atctttccag gctttggtgg cccaagagca gtctgggtgg atggaagtgg 840
ctgtcccctc ctctccagcc cctgcccacc cactggtgga ggtgctaact agcagggacg 900
tggcatagga tgggagctgg gcgtgaggtg cttggggtcc attctttgtc cctcagettc 960
teagagteeg geeageeett gtgtteeegt geeceaeact tteeteetee ceaetgeagt 1020
gaggcaatag teeggggtgg ggeetggeet ecetgeeetg attggggaet caggaggtga 1080
ggeetggggg getteetgee eceteettge ceaectgeet geeceeggge ageaegggag 1140
ggagagcagg gtgagcacgc ttgttggttt cagatgcact ttctgcttgc attgccgtat 1200
ctgtgcgttc cttcatcctg gtcctggctt tatggaacac catgttttta gcatgttttt 1260
<210> 136
<211> 62
<212> PRT
<213> Homo sapiens
<400> 136
Met Cys Asn Leu Pro Glu Asn Leu Phe Cys Phe Trp Ser Thr Ser Gly
                                    10
Val Ala Ser Gly Pro Arg Ala Phe Ala Thr Val Leu Pro Pro Ala Pro
                                25
Thr Ser Ser Val Cys Leu Gln Ser Leu Ile Tyr Arg Ser Pro Arg Cys
                            40
Leu Leu Tyr Ser Leu Cys Ala Trp Pro Phe Cys Tyr Leu Ala
                        55
<210> 137
<211> 1330
<212> DNA
<213> Homo sapiens
<400> 137
aagettggea egagggaage eeateeaggt catgtgetae gaetatgaea atgaeggggg 60
ccatgactic ateggegagt tecagacete agtgteacag atgtgtgagg etegagacag 120
cgtcccgctg gagttcgagt gcatcaaccc caagaagcag aggaagaaga agaactataa 180
aaactcgggc atcatcatcc tgcgatcctg caagataaac cgagactact ccttccttga 240
ctacatcctg ggaggctgcc agctcatgtt caccgttgga atagacttta cagcctccaa 300
cgggaatece etegaceett cetetttgea etatateaac eetatgggea eeaacgaata 360
tetgteggee atetgggetg ttgggeagat catteaggae tacgacagtg ataagatgtt 420
tecagetetg ggattegggg eccagttace eccagaetgg aagteteeca tgagtttgee 480
atcaacttca accccaccaa ccccttctgc tcaggtgtgg atggtattgc ccaggcgtac 540
tragettgcc tgcccacat cegettetac ggtcctacca atttetecce categtcaac 600
cacgtggccc ggtttgcggc ccaggccaca caacagcgga cggccacgca gtacttcatc 660
ctcctcatca tcacggacgg ggtcatcagt gacatggagg agacacggca tgccgtggtg 720
caggetteca agetgeecat gtecateate ategtgggeg tgggeaatge ggaetteget 780
gccatggagt tcctggatgg ggacagccgc atgctgcgct cccacacggg ggaggaggca 840
gcccgcgata ttgtgcagtt cgttcccttt cgagagttcc gcaacgcagc aaaagagacc 900
ttggccaaag ctgtgctggc ggagctgccc caacaagttg tgcagtattt caagcataaa 960
aacctgcccc ccaccaactc ggagcccgcc tgagctccag tgcccagcag cagcatgtca 1020
gctgagcetc etgecetecc ccaggaacat gcacgetcac tetgetteet tgtgggtggc 1080
ctttttttac cgatcccctt ttttatttt tacaaccgga cctccacccc caacttcctc 1140
cagcocagot gggottoott tgttggagto aactgttgat gottocaggo caaactggot 1200
tectetecte etetececae etttgecatt ettaagtatt gaatgtactt tgtataattt 1260
```

aaaaaaaaa <210> 138 <211> 423 <212> PRT <213> Homo sapiens <400> 138 Met Cys Tyr Asp Tyr Asp Asn Asp Gly Gly His Asp Phe Ile Gly Glu . 10 Phe Gln Thr Ser Val Ser Gln Met Cys Glu Ala Arg Asp Ser Val Pro 25 Leu Glu Phe Glu Cys Ile Asn Pro Lys Lys Gln Arg Lys Lys Asn 40 Tyr Lys Asn Ser Gly Ile Ile Ile Leu Arg Ser Cys Lys Ile Asn Arg Asp Tyr Ser Phe Leu Asp Tyr Ile Leu Gly Gly Cys Gln Leu Met Phe . 70 Thr Val Gly Ile Asp Phe Thr Ala Ser Asn Gly Asn Pro Leu Asp Pro 85 90 Ser Ser Leu His Tyr Ile Asn Pro Met Gly Thr Asn Glu Tyr Leu Ser 105 Ala Ile Trp Ala Val Gly Gln Ile Ile Gln Asp Tyr Asp Ser Asp Lys 120 Met Phe Pro Ala Leu Gly Phe Gly Ala Gln Leu Pro Pro Asp Trp Lys 135 Ser Pro Met Ser Leu Pro Ser Thr Ser Thr Pro Pro Thr Pro Ser Ala 150 155 Gln Val Trp Met Val Leu Pro Arg Arg Thr Gln Leu Ala Cys Pro Thr 170 Ser Ala Ser Thr Val Leu Pro Ile Ser Pro Pro Ser Ser Thr Thr Trp 180 185 Pro Gly Leu Arg Pro Arg Pro His Asn Ser Gly Arg Pro Arg Ser Thr 200 Ser Ser Ser Ser Ser Ser Arg Thr Gly Ser Ser Val Thr Trp Arg Arg 215 His Gly Met Pro Trp Cys Arg Leu Pro Ser Cys Pro Cys Pro Ser Ser 230 235 Ser Trp Ala Trp Ala Met Arg Thr Ser Leu Pro Trp Ser Ser Trp Met 245 250

Gly Thr Ala Ala Cys Cys Ala Pro Thr Arg Gly Arg Arg Gln Pro Ala 260 265 270

Ile Leu Cys Ser Ser Phe Pro Phe Glu Ser Ser Ala Thr Gln Gln Lys Arg Pro Trp Pro Lys Leu Cys Trp Arg Ser Cys Pro Asn Lys Leu Cys 295 Ser Ile Ser Ser Ile Lys Thr Cys Pro Pro Pro Thr Arg Ser Pro Pro 310 315 Glu Leu Gln Cys Pro Ala Ala Ala Cys Gln Leu Ser Leu Leu Pro Ser 330 325 Pro Arg Asn Met His Ala His Ser Ala Ser Leu Trp Val Ala Phe Phe 345 Tyr Arg Ser Pro Phe Leu Phe Phe Thr Thr Gly Pro Pro Pro Pro Thr Ser Ser Ser Pro Ala Gly Leu Pro Leu Leu Glu Ser Thr Val Asp Ala 375 380 Ser Arg Pro Asn Trp Leu Pro Leu Leu Leu Ser Pro Pro Leu Pro Phe 395 390 Leu Ser Ile Glu Cys Thr Leu Tyr Asn Phe Ser Gly Ile Val Ile Glu 410 Asn Lys Ile Phe Thr Ile Ile 420

<210> 139 <211> 1920 <212> DNA

<213> Homo sapiens

#### <400> 139

aagettggea egagggegga gaeggeggag egggeetttt ggegteeact gegeggetge 60 accetgeece atcetgeegg gateatggte tgeggeagee egggagggat getgetgetg 120 egggeeggge tgettgeeet ggetgetete tgeetgetee gggtgeeegg ggeteggget 180 gragectgtg agreegterg catercettg tgraagters tgreetggaa catgartaag 240 atgeceaace acetgeacea cageacteag gecaaegeca teetggecat egageagtte 300 gaaggtetge tgggeaccca etgeageecc gatetgetet tetteetetg tgeeatgtae 360 gegeceatet geaccattga ettecageae gageceatea agecetgtaa gtetgtgtge 420 gagegggeee ggeagggetg tgageceata eteateaagt acegecaete gtggeeggag 480 aacctggcct gcgaggagct gccagtgtac gacaggggcg tgtgcatctc tcccgaggcc 540 atcgttactg cggacggagc tgattttcct atggattcta gtaacggaaa ctgtagaggg 600 gcaagcagtg aacgctgtaa atgtaagcct attagagcta cacagaagac ctatttccgg 660 aacaattaca actatgtcat togggotaaa gttaaagaga taaagactaa gtgocatgat 720 gtgactgcag tagtggaggt gaaggagatt ctaaagtcct ctctggtaaa cattccacag 780 gacactgtca acctctatac cagctctggc tgcctctgcc ctccacttaa tgttaatgag 840 gaatatatca tcatgggcta tgaagatgag gaacgttcca gattactctt ggtggaaggc 900 tctatagctg agaagtggaa ggatcgactc ggtaaaaaaag ttaagcgctg ggatatgaag 960 cttcgtcatc ttggactcag taaaagtgat tctagcaata gtgattccac tcagagtcag 1020 aagtetggca ggaactegaa ceeeeggcaa geacgeaact aaateeegaa atacaaaaaag 1080 taacacagtg gacttcctat taagacttac ttgcattgct ggactagcaa aggaaaattg 1140 cactattgca catcatattc tattgtttac tataaaaatc atgtgataac tgattattac 1200 ttotgtttct cttttggttt ctgcttctct cttctctcaa cccctttgta atggtttggg 1260 ggcagactet taagtatatt gtgagtttte tattteacta atcatgagaa aaactgttet 1320 tttgcaataa taataaatta aacatgctgt taccagagcc tctttgctgg agtctccaga 1380

tgttaattta ctttctgcac cccaattggg aatgcaatat tggatgaaaa gagaggtttc 1440 tggtattcac agaaagctag atatgcctta aaacatactc tgccgatcta attacagcct 1500 tatttttgta tgccttttgg gcattctcct catgcttaga aagttccaaa tgtttataaa 1560 ggtaaaatgg cagtttgaag tcaaatgtca cataggcaaa gcaatcaagc accaggaagt 1620 gtttatgagg aaacaacacc caagatgaat tatttttgag actgtcagga agtaaaataa 1680 ataggagett aagaaagaac attttgeetg attgagaage acaaetgaaa ceagtageeg 1740 ctggggtgtt aatggtagca ttcttctttt ggcaatacat ttgatttgtt catqaatata 1800 ttaatcagca ttagagaaat gaattataac tagacatctg ctgttatcac catagttttg 1860 tttaatttgc ttccttttaa ataaacccat tggtgaaagt caaaaaaaaa aaaaaaaaa 1920 <210> 140 <211> 325 <212> PRT <213> Homo sapiens <400> 140 Met Val Cys Gly Ser Pro Gly Gly Met Leu Leu Leu Arg Ala Gly Leu Leu Ala Leu Ala Ala Leu Cys Leu Leu Arg Val Pro Gly Ala Arg Ala 20 25 Ala Ala Cys Glu Pro Val Arg Ile Pro Leu Cys Lys Ser Leu Pro Trp 40 Asn Met Thr Lys Met Pro Asn His Leu His His Ser Thr Gln Ala Asn 55 Ala Ile Leu Ala Ile Glu Gln Phe Glu Gly Leu Leu Gly Thr His Cys 70 Ser Pro Asp Leu Leu Phe Phe Leu Cys Ala Met Tyr Ala Pro Ile Cys Thr Ile Asp Phe Gln His Glu Pro Ile Lys Pro Cys Lys Ser Val Cys 100 105 Glu Arg Ala Arg Gln Gly Cys Glu Pro Ile Leu Ile Lys Tyr Arg His 120 Ser Trp Pro Glu Asn Leu Ala Cys Glu Glu Leu Pro Val Tyr Asp Arg 135 Gly Val Cys Ile Ser Pro Glu Ala Ile Val Thr Ala Asp Gly Ala Asp 150 155 Phe Pro Met Asp Ser Ser Asn Gly Asn Cys Arg Gly Ala Ser Ser Glu Arg Cys Lys Cys Lys Pro Ile Arg Ala Thr Gln Lys Thr Tyr Phe Arg 185 Asn Asn Tyr Asn Tyr Val Ile Arg Ala Lys Val Lys Glu Ile Lys Thr 195 200 205 Lys Cys His Asp Val Thr Ala Val Val Glu Val Lys Glu Ile Leu Lys 215 Ser Ser Leu Val Asn Ile Pro Gln Asp Thr Val Asn Leu Tyr Thr Ser

235

230

```
Ser Gly Cys Leu Cys Pro Pro Leu Asn Val Asn Glu Glu Tyr Ile Ile
                                  250
Met Gly Tyr Glu Asp Glu Glu Arg Ser Arg Leu Leu Val Glu Gly
                             . 265
            260
Ser Ile Ala Glu Lys Trp Lys Asp Arg Leu Gly Lys Lys Val Lys Arg
                            280
Trp Asp Met Lys Leu Arg His Leu Gly Leu Ser Lys Ser Asp Ser Ser
Asn Ser Asp Ser Thr Gln Ser Gln Lys Ser Gly Arg Asn Ser Asn Pro
305
                    310
                                       315
Arg Gln Ala Arg Asn
                325
<210> 141
<211> 1469
<212> DNA
<213> Homo sapiens
<400> 141
gatagettgg cacgaggetg ggaagtagag gtgttgtget gageggeget eggegaactg 60
tgtggaccgt ctgctgggac tccggccctg cgtccgctca gccccgtggc cccgcgcacc 120
tactgccatg gagacgcggc ctcgtctcgg ggccacctgt ttgctgggct tcagtttcct 180
gctcctcgtc atctcttctg atggacataa tgggcttgga aagggttttg gagatcatat 240
tcattggagg acactggaag atgggaagaa agaagcagct gccagtggac tgcccctgat 300
ggtgattatt cataaatcct ggtgtggagc ttgcaaagct ctaaagccca aatttgcaga 360
atctacggaa atttcagaac tctcccataa ttttgttatg gtaaatcttg aggatgaaga 420
ggaacccaaa gatgaagatt tcagccctga cgggggttat attccacgaa tcctttttct 480
ggatcccagt ggcaaggtgc atcctgaaat catcaatgag aatggaaacc ccagctacaa 540
gtatttttat gtcagtgccg agcaagttgt tcaggggatg aaggaagctc aggaaaggct 600
gacgggtgat gccttcagaa agaaacatct tgaagatgaa ttgtaacatg aatgtgcccc 660
ttctttcatc agagttagtg ttctggaagg aaagcagcag ggaagggaat attgaggaat 720
catctagaac aattaagccg accaggaaac ctcattccta cctacactgg aaggagcgct 780
ctcactgtgg aagagttctg ctaacagaag ctggtctgca tgtttgtgga tccagcggag 840
agtggcagac tttcttctcc:ttttccctct cacctaaatg tcaacttgtc attgaatgta 900
aagaatgaaa ccttctgaca caaaacttga gccacttgga tgtttactcc tcgcacttaa 960
gtatttgagt cttttcccat ttcctccac tttactcacc ttagtggtga aaggagacta 1020
gtagcatctt ttctacaacg ttaaaattgc agaagtagct tatcattaaa aaacaacaac 1080
aacaacaata acaataaatc ctaagtgtaa atcagttatt ctacccccta ccaaggatat 1140
cagectgttt tttecetttt tteteetggg aataattgtg ggettettee caaattteta 1200
cagcetettt cetettetea tgettgaget tecetgtttg caegeatgeg tgtgeaggae 1260
tggctgtgtg cttggactcg gctccaggtg gaagcatgct ttcccttgtt actgttggag 1320
aaactcaaac cttcaagccc taggtgtagc cattttgtca agtcatcaac tgtatttttg 1380
tactggcatt aacaaaaaaa gagataaaat attgtaccat taaactttaa taaaacttta 1440
aaaggaaaaa aaaaaaaaa aaaaaaaaa
<210> 142
<211> 172
<212> PRT
<213> Homo sapiens
Met Glu Thr Arg Pro Arg Leu Gly Ala Thr Cys Leu Leu Gly Phe Ser
                                    10
```

Phe Leu Leu Leu Val Ile Ser Ser Asp Gly His Asn Gly Leu Gly Lys 20 . 25 Gly Phe Gly Asp His Ile His Trp Arg Thr Leu Glu Asp Gly Lys Lys 40 Glu Ala Ala Ser Gly Leu Pro Leu Met Val Ile Ile His Lys Ser Trp Cys Gly Ala Cys Lys Ala Leu Lys Pro Lys Phe Ala Glu Ser Thr 70 Glu Ile Ser Glu Leu Ser His Asn Phe Val Met Val Asn Leu Glu Asp Glu Glu Glu Pro Lys Asp Glu Asp Phe Ser Pro Asp Gly Gly Tyr Ile 105 Pro Arg Ile Leu Phe Leu Asp Pro Ser Gly Lys Val His Pro Glu Ile . 115 120 Ile Asn Glu Asn Gly Asn Pro Ser Tyr Lys Tyr Phe Tyr Val Ser Ala 135 Glu Gln Val Val Gln Gly Met Lys Glu Ala Gln Glu Arg Leu Thr Gly 155 150 160 Asp Ala Phe Arg Lys Lys His Leu Glu Asp Glu Leu 165 <210> 143 <211> 1458 <212> DNA <213> Homo sapiens <400> 143 totagaacta gtggatcccc cgggctgcag gaattcggca cgagcttcaa gtgaccattc 60 tttttcttct gcccagtatt tgcagcagta acagcacagg tgttttagag gcagctaata 120 atteactigt tactacaaca aaaccateta taacaacace aaacacagaa teattacaga 180 aaaatgttgt cacaccaaca actggaacaa ctcctaaagg aacaatcacc aatgaattac 240 ttaaaatgtc tctgatgtca acagctactt ttttaacaag taaagatgaa ggattgaaag 300 ccacaaccac tgatgtcagg aagaatgact ccatcatttc aaacgtaaca gtaacaagtg 360 ttacacttcc aaatgctgtt tcaacattac aaagttccaa acccaagact gaaactcaga 420 gttcaattaa aacaacagaa ataccaggta gtgttctaca accagatgca tcaccttcta 480 aaactggtac attaacctca ataccagtta caattccaga aaacacctca cagtctcaag 540 taataggcac tgagggtgga aaaaatgcaa gcacttcagc aaccagccgg tcttattcca 600 gtattatttt geeggtggtt attgetttga ttgtaataac acttteagta tttgttetgg 660

Egggtttgta ccgaatgtg tggaaggcag atccgggcac accagaaaat ggaaatgatc 720 aacctcagtc tgataaagag agcgtgaagc ttcttaccgt taagacaatt tctcatgagt 780 ctggtgagca ctctgcacaa ggaaaaacca agaactgaca gcttgaggaa ttctctcac 840 acctaggcaa taattacgct taatcttcag cttctatgca ccaagcgtgg aaaaggagaa 900 agtcctgcag aatcaatccc gacttccata cctgctgctg gactgtacca gacgtctgtc 960 ccagtaaagt gatgtccagc tgacatgcaa taatttgatg gaatcaaaaa gaaccceggg 1020 gctctcctgt tctctcacat ttaaaaattc cattactca tttacaggag cgttcctagg 1080 aaaaggaatt ttaggaggag aatttgtgag cagtgaatct gacagccag gaggtgggct 1140 cgctgatagg catgacttc cctactttc tcggtgttct tatatacct actgtcagta tttattgtc 1260 accactatgt taatgcagg aaaagttgca cgtgtattat taaaatttag gtagaatca 1320

taccatgcta ctttgtacat ataagtattt tattcctgct ttcgtgttac ttttaataaa 1380 taactactgt actcaatact ctaaaaaatac tataacatga Ctgtgaaaaa aaaaaaaaaa 1440 aaaaaaaaaa aaaaaaaaa aaaaaaaaa 1458

<210> 144

<211> 255

<212> PRT

<213> Homo sapiens

<400> 144

Val Thr Ile Leu Phe Leu Pro Ser Ile Cys Ser Ser Asn Ser Thr
1 5 10 15

Gly Val Leu Glu Ala Ala Asn Asn Ser Leu Val Thr Thr Thr Lys Pro \$20\$ \$25\$ \$30

Ser Ile Thr Thr Pro Asn Thr Glu Ser Leu Gln Lys Asn Val Val Thr 35 40 45

Pro Thr Thr Gly Thr Thr Pro Lys Gly Thr Ile Thr Asn Glu Leu Leu 50 55 60

Lys Met Ser Leu Met Ser Thr Ala Thr Phe Leu Thr Ser Lys Asp Glu 65 70 75 80

Ser Asn Val Thr Val Thr Ser Val Thr Leu Pro Asn Ala Val Ser Thr

Leu Gln Ser Ser Lys Pro Lys Thr Glu Thr Gln Ser Ser Ile Lys Thr

Thr Glu Ile Pro Gly Ser Val Leu Gln Pro Asp Ala Ser Pro Ser Lys 130 135 140

Thr Gly Thr Leu Thr Ser Ile Pro Val Thr Ile Pro Glu Asn Thr Ser 145 150 155 160

Gln Ser Gln Val Ile Gly Thr Glu Gly Gly Lys Asn Ala Ser Thr Ser 165 170 175

Ala Thr Ser Arg Ser Tyr Ser Ser Ile Ile Leu Pro Val Val Ile Ala 180 185 190

Leu Ile Val Ile Thr Leu Ser Val Phe Val Leu Val Gly Leu Tyr Arg 195 200 205

Met Cys Trp Lys Ala Asp Pro Gly Thr Pro Glu Asn Gly Asn Asp Gln 210 215 220

Pro Gln Ser Asp Lys Glu Ser Val Lys Leu Leu Thr Val Lys Thr Ile 225 230 235 240

Ser His Glu Ser Gly Glu His Ser Ala Gln Gly Lys Thr Lys Asn 245 250 250

<210> 145

<211> 839 <212> DNA <213> Homo sapiens <400> 145 ggaacagcgt aagaggagag agacacattc agcagccaaa ggactcggtg gaaagagcag 60 aacaccatag acaatatgtc gctcttggga cccaaggtgc tgctgtttct tgctgcattc 120 atcatcacct ctgactggat acccctgggg gtcaatagtc aacgaggaga cgatgtgact 180 caagegacte cagaaacatt cacagaagat cetaatetgg tgaatgatee egetacagat 240 gaaacagttt tggctgtttt ggctgatatt gcaccttcca cagatgactt ggcctccctc 300 aqtqaaaaaa ataccactgc agagtgctgg gatgagaaat ttacctgcac aaggctctac 360 tetgtgcate ggccggttaa acaatgcatt catcagttat gcttcaccag tttacgacgt 420 atgtacatcg tcaacaagga gatctgctct cgtcttgtct gtaaggaaca cgaagctatg 480 aaagatgagc tttgccgtca gatggctggt ctgcccccta ggagactccg tcgctccaat 540 tactteegae tteeteectg tgaaaatgtg gatttgeaga gacceaatgg tetgtgatea 600 ttgaaaaaga ggaaagaaga aaaaatgtat gggtgagagg aaggaggatc tccttcttct 660 ccaaccattg acagetaacc cttagacagt atttettaaa ccaatcettt tgcaatgtec 720 agettttace cetactetet aettttteae ceaaactgat aacatttate teatttteta 780 <210> 146 <211> 173 <212> PRT <213> Homo sapiens <400> 146 Met Ser Leu Leu Gly Pro Lys Val Leu Leu Phe Leu Ala Ala Phe Ile · 10 Ile Thr Ser Asp Trp Ile Pro Leu Gly Val Asn Ser Gln Arg Gly Asp Asp Val Thr Gln Ala Thr Pro Glu Thr Phe Thr Glu Asp Pro Asn Leu 40 Val Asn Asp Pro Ala Thr Asp Glu Thr Val Leu Ala Val Leu Ala Asp 55 Ile Ala Pro Ser Thr Asp Asp Leu Ala Ser Leu Ser Glu Lys Asn Thr 70 Thr Ala Glu Cys Trp Asp Glu Lys Phe Thr Cys Thr Arg Leu Tyr Ser 90 Val His Arg Pro Val Lys Gln Cys Ile His Gln Leu Cys Phe Thr Ser Leu Arg Arg Met Tyr Ile Val Asn Lys Glu Ile Cys Ser Arg Leu Val 120 Cys Lys Glu His Glu Ala Met Lys Asp Glu Leu Cys Arg Gln Met Ala 135 Gly Leu Pro Pro Arg Arg Leu Arg Arg Ser Asn Tyr Phe Arg Leu Pro 145 150 Pro Cys Glu Asn Val Asp Leu Gln Arg Pro Asn Gly Leu

170

165

```
<210> 147
<211> 2227
<212> DNA
<213> Homo sapiens
<400> 147
tgagacagaa ggttgtgttg gggaactgaa ggagtttctg tgggcggaca gggaaccctg 60
egittetact gigtgattet gecaecitee iggeeegaeg ceaigggagt gaetigigig 120
teccagatge etgtggeega gggeaagagt gtteageaaa eegtagaget eettaeeegg 180
aaattggaga tgcttggggc agagaagcaa ggaacatttt gtgtggactg tgagacttac 240
catacggccg cctctaccct tggcagccaa ggtggagtat ggcccctgtg tggtagctag 300
tgactgctgg agtctgctgc tcgagttcct acagagtttt ctaggcagcc acacaccagg 360
ggctcccgca gtgtttggga acagacatga tgcggtctac ggcccagcag ataccatggt 420
ccagtacatg gaactettea acaagateeg caageageag caggtgeegg tggetgggat 480
tcgttagtga tgagcagctg ccagctgagc tctgtcacca ggggtactcc acaggaggag 540
caggtgctga ctttcaggtc cctggacccc agaaacccag ggtagacatg gactctactc 600
teettetetg gtteteaget gtggettttg ttetgggget gagteeete eecaaceec 660
tgacteteac acatageeec ceateagetg ttttacteeg tgeettactg gatttggeet 720
gtcctcaaga atggtaatta tgaagagtgg agaagtttgg accttgcctc ctttaaggga 780
aaggtaggac acgaatgtcc ctgtctggta ctggtggggg aaatagtccg tatccccaac 840
tattaaggat ttgtcccagg ccaatggtga acatgctgca ttttatgttt ggattgtgct 900
gtaataagag cotottoott cootcagagg atgtggctgg gottotatoc tagagatgga 960
gtagaaggca caactggttt gatagttact attttctgac ctgtttgctg aagtgatttg 1020
cgaattgact ttcctagggt gttgcctgag tcctttgaaa tctccttctg acatctttcc 1080
cttctgttgt gaaatatgtt aagccacagg Ccaaactgct ataagatcga agtttgtttt 1140
tttctcacct aataatagag aggtaatcag atggtctagg gcagatttaa ctctacaagg 1200
ttatcaggaa ctttgtttcc ttctgtctta ttcagccatt cccagtatgt tttcttaccc 1260
ataagatcaa agcagactca tcagctccat atctgcattc cactggggaa agagagagag 1320
aaaagagcag attitaaaaa aaagatatga Ctgagcattg ctcagatcac tgtggccaca 1380
ctttgctgaa agagatgctg ggacatagaa Cctcttatct gggcagtcat gtgctgagtt 1440
aaaactcagg gattctgtga ctacaagatg aaagacaatt tggttgctga gatgcagtta 1500
atggettetg ttacatggag etcaatggae gtgeeeagga atgettttgg etgttatttt 1560
gcagttaata cctcctgtaa ctaaagcatt tgtttatgag ttgacttgag agaagggctg 1620
atctcagage egetttgage taagttggat tagtcacact aggaagttaa ttecacacet 1680
ttcgtctaag tctcagtatt gaggcctctc Cagttctcat gcaccctgat cttagggtta 1740
gaatacttga cootgataco tgcaccatgo ttcatggtto otgagotott totootgttt 1800
catttgagcc tecaaactac atatttggtc atattgcctg cetaceccat geetgetgca 1860
gaaatattca tccaggttaa ccttgatata cacagagatg gtcttggaga attgtgaatg 1920
tatgtactgt attgtcatca aggatactgt cccttatttg aaggcatcta aagagaaact 1980
gttttcagat ccaagtgctc agatctaaag Cctctgcaac aagtcaggtg gtggtcatgt 2040
ttcccttcta gttttggctg acaggaagct Cagttcagta ccataactac agaacctgtc 2100
atctgtattt tittgttctca coccgttttt gttattttgt ttctggtttt ttatattgag 2160
gtatgtttta gatatagttt acaaaaataa aacgcacaga tcttaaaaaa aaaaaaaaa 2220
aaaaaaa
<210> 148
<211> 116
<212> PRT
<213> Homo sapiens
<400> 148
Met Met Arg Ser Thr Ala Gln Gln Ile Pro Trp Ser Ser Thr Trp Asn
                                    10
Ser Ser Thr Arg Ser Ala Ser Ser Ser Arg Cys Arg Trp Leu Gly Phe
                                 25
Val Ser Asp Glu Gln Leu Pro Ala Glu Leu Cys His Gln Gly Tyr Ser
```

Thr Gly Gly Ala Gly Ala Asp Phe Gln Val Pro Gly Pro Gln Lys Pro 55 Arg Val Asp Met Asp Ser Thr Leu Leu Leu Trp Phe Ser Ala Val Ala Phe Val Leu Gly Leu Ser Pro Leu Pro Asn Pro Leu Thr Leu Thr His 85 90 Ser Pro Pro Ser Ala Val Leu Leu Arg Ala Leu Leu Asp Leu Ala Cys Pro Gln Glu Trp 115 <210> 149 <211> 983 <212> DNA <213> Homo sapiens <400> 149 ggcacgaggg eccggetect geagacgete ggcetecget catteetgae eccgeagtgg 60 gegegatgge ggaggetgta etgagggteg eeeggeggea getgageeag egeggegggt-120 etggagecee eatecteetg eggeagatgt tegageetgt gagetgeace tteaegtace 180 tgctgggtga cagagagtcc cgggaggccg ttctgatcga cccagtcctg gaaacagcgc 240 ctegggatge ceagetgate aaggagetgg ggetgegget getetatget gtgaatacee 300 actgccacgc ggaccacatt acaggctcgg ggctgctccg ttccctcctc cctggctgcc 360 agtetgteat etceegeett agtggggeec aggetgaett acacattgag gatggagaet 420 ccatccgctt cgggcgcttc gcgttggaga ccagggccag ccctggccac accccaggct 480 gtgtcacctt cgtcctgaat gaccacagca tggccttcac tggagatgcc ctgttgatcc 540 gtgggtgtgg gcggacagac ttccagcaag gctgtgccaa gaccttgtac cactcggtcc 600 atgaaaagat cttcacactt ccaggagact gtctgatcta ccctgctcac gattaccatg 660 ggttcacagt gtccaccgtg gaggaggaga ggactctgaa ccctcggctc accctcagct 720 gtgaggagtt tgtcaaaatc atgggcaacc tgaacttgcc taaacctcag cagatagact 780 ttgctgttcc agccaacatg cgctgtgggg tgcagacacc cactgcctga tctcacttct 840 gtcagatgct cccatccact attaatgcac taggtgggag gagagggcgg caatgacact 900 geacetetee titteecaceq catteectgg ageteectaa ataaaactit tittaacgig 960 983 aaaaaaaaa aaaaaaaaaa aaa <210> 150 <211> 254 <212> PRT <213> Homo sapiens <400> 150 Met Ala Glu Ala Val Leu Arg Val Ala Arg Arg Gln Leu Ser Gln Arg 1 5 10 Gly Gly Ser Gly Ala Pro Ile Leu Leu Arg Gln Met Phe Glu Pro Val . 25 Ser Cys Thr Phe Thr Tyr Leu Leu Glÿ Asp Arg Glu Ser Arg Glu Ala 40 Val Leu Ile Asp Pro Val Leu Glu Thr Ala Pro Arg Asp Ala Gln Leu 55 Ile Lys Glu Leu Gly Leu Arg Leu Leu Tyr Ala Val Asn Thr His Cys

75

70

His Ala Asp His Ile Thr Gly Ser Gly Leu Leu Arg Ser Leu Leu Pro 90 Gly Cys Gln Ser Val Ile Ser Arg Leu Ser Gly Ala Gln Ala Asp Leu 105 His Ile Glu Asp Gly Asp Ser Ile Arg Phe Gly Arg Phe Ala Leu Glu 115 120 Thr Arg Ala Ser Pro Gly His Thr Pro Gly Cys Val Thr Phe Val Leu Asn Asp His Ser Met Ala Phe Thr Gly Asp Ala Leu Leu Ile Arg Gly 155 150 Cys Gly Arg Thr Asp Phe Gln Gln Gly Cys Ala Lys Thr Leu Tyr His 170 Ser Val His Glu Lys Ile Phe Thr Leu Pro Gly Asp Cys Leu Ile Tyr 185 Pro Ala His Asp Tyr His Gly Phe Thr Val Ser Thr Val Glu Glu 200 Arg Thr Leu Asn Pro Arg Leu Thr Leu Ser Cys Glu Glu Phe Val Lys 215 Ile Met Gly Asn Leu Asn Leu Pro Lys Pro Gln Gln Ile Asp Phe Ala . 235 Val Pro Ala Asn Met Arg Cys Gly Val Gln Thr Pro Thr Ala 245

<210> 151 <211> 1254 <212> DNA <213> Homo sapiens

#### <400> 151

tgggctggaa cgcgccggaa tctgaggtgt gagtagagcc tgggggagag tggatccagg 60 tgaagggggc agaggactgg gagttttcgt cctcttgaat aagaactcga caacagagtg 120 ggaactttct gtcttgtgat ccattgcctg gtgagtcaca gctcacacca tggatttaac 180 etgagagett caacttetge tttggeeetg gagtteeeat geeetggtgt ettetaceag 240 ttcttagtgt gtcgcactgg agcacagagg acactcgatc gtgcggcgcg cagggcgggg 300 ggccgccgct gcctccccgc gggatggctg gcactgtgct cggagtccgt gcgggcgtgt 360 teatettage eetgetetgg gtggeagtge tgetgetgtg tgtgetgetg teeagageet 420 ccggggcggc gaggttetet gteatttttt tattettegg tgetgtgate ateacattag 480 ttetgttget ttteeegega getggtgaat teeeageece agaagtggaa gttaagattg 540 tggatgactt tttcattggc cgctatgtcc tgctggcttt ccttagtgcc atcttccttg 600 gaggeetett ettggtttta acceattatg ttetggagee gatgtatgee aaaceaetge 660 actectactg accaetette aggaaaaega aaacatgtte teteetteat tgtgatgaca 720 ttgatgagca ggaaggcact attcagagcc ttgttttgac agccctcatg ccttaaggtt 780 agaggagtat ctgtccatca ctaagacaaa tctctggagt cctggcttcc agaaacagga 840 ttgccaaatt gtccctgtgg ggctagattc ttaccagctt aagaaggata ttgctatctt 900 cttagtaccc gtaccttagg atttccaact gttttgaaag ggaaatagta acagtgatct 960 gcttagagtg gattttcact caagtcctta gtaagtggat tggggaaaaa agcacatggg 1020 cttctqqttc tttttqataa tacataaaat tattcattat gaggttqcaq ttqtttqcaa 1080 aggagaggca ctcaaatttg aaaggttatt ttaatgtgat aatttggaag acttactcag 1140

atgttggtca ttgaccactc tgtgcatata tttctgcaga gctctgtgaa ggcaatgagt 1200 gtcacttccc tctgctctaa taaagcaata aataataaaa aaaaaaaaa aaaa <210> 152 <211> 150 <212> PRT <213> Homo sapiens <400> 152 Met Pro Trp Cys Leu Leu Pro Val Leu Ser Val Ser His Trp Ser Thr 5 10 Glu Asp Thr Arg Ser Cys Gly Ala Gln Gly Gly Gly Pro Pro Leu Pro 25 Pro Arg Gly Met Ala Gly Thr Val Leu Gly Val Arg Ala Gly Val Phe 40 . Ile Leu Ala Leu Leu Trp Val Ala Val Leu Leu Leu Cys Val Leu Leu Ser Arg Ala Ser Gly Ala Ala Arg Phe Ser Val Ile Phe Leu Phe Phe 70 Gly Ala Val Ile Ile Thr Leu Val Leu Leu Phe Pro Arg Ala Gly 90 Glu Phe Pro Ala Pro Glu Val Glu Val Lys Ile Val Asp Asp Phe Phe 105 Ile Gly Arg Tyr Val Leu Leu Ala Phe Leu Ser Ala Ile Phe Leu Gly 120 Gly Leu Phe Leu Val Leu Ile His Tyr Val Leu Glu Pro Met Tyr Ala 135 Lys Pro Leu His Ser Tyr 145 <210> 153 <211> 1803 <212> DNA <213> Homo sapiens <400> 153 aaaatcattc ctgatggact tcatgttgag atacatgtac aaccaggaat cagttgattg 60 ggttggagac tacaatgaac cattgactgg tttttcatgg agaggtggat ctgaacgaga 120 gaccacagga attcagatat ggagtgaaat cttccttatc aataaacctg atggtaaaaa 180 ggttgcagtg ttattgatgg atactcaggg aacctttgat agtcagtcaa ctttgagaga 240 ttcagccaca gtatttgccc ttagcacaat gatcagctca atacaggtat ataacttatc 300 ccaaaatgtc caggaggatg atcttcagca cctccagctt ttcactgagt atggcagact 360 ggcaatggag gaaacattcc tgaagccatt tcagagtctg atatttcttg ttcgagactg 420 gagtttccca tacgaatttt catatggagc cgatggtggt gccaaattct tggaaaaacg 480 cctcaaggtc tcagggaacc agcatgaaga actacagaac gtcagaaaac acatccattc 540 ctgtttcacc aacatttcct gttttctgct acctcatcct ggcttaaaag tagctaccaa 600 tccaaacttt gatggaaaat tgaaagaaat agatgatgaa ttcatcaaaa acttgaaaat 660 actgattcct tggctactta gtcccgagag cctagatatt aaagagatca atgggaataa 720 aatcacctgc cggggtctgg tggagtactt caaggcttat ataaagatct atcaaggtga 780

agaattacca catcccaaat ccatgttaca ggccacagca gaagctaaca atttagcagc 840

```
cgtggcaact gccaaggaca catacaacaa aaaaatggaa gagatttgtg gtggtgacaa 900
accatttetg geoceaaatg acttgeagae caaacaeetg caaettaagg aagaatetgt 960
gaagctattc cgaggggtga agaagatggg tggggaagaa tttagccggc gttacctgca 1020
gcagttggag agtgaaatag atgaacttta catccaatat atcaagcaca atgatagcaa 1080
aaatatotto catgoagoto gtaccocago cacactgttt gtagtoatot ttatcacata 1140
tgtgattgct ggtgtgactg gattcattgg tttggacatc atagctagcc tatgcaatat 1200
gataatggga ctgaccctta tcaccctgtg cacttgggca tatatccggt actctggaga 1260
ataccgagag ctgggagctg taatagacca ggtggctgca gctctgtggg accagggaag 1320
tacaaatgag getttgtaca agetttacag tgcagcagca acccacagac atetgtatca 1380
tcaagctttc cctacaccaa agtcggaatc tactgaacaa tcagaaaaga aaaaaatgta 1440
atgcaaattt taagaaatac aggtgcatga ccaattgtca attaaatatt cagttttatg 1500
totocatgoa aacattoaaa gtgottocat cagaacggag taaaatacta aacacctotg 1560
aagactgcaa actggattag ttcttttact tcagtgttta ataagcagat gtatgtatgc 1620
atggttatac tattttgtta acatgtacaa tttcctgatt tttcttcaaa aatgctgtta 1680
taaagtattt gtctatttat gataacagta cacgtgttct gcttgaattt actaaattct 1740
<210> 154
<211> 475
<212> PRT
<213> Homo sapiens
<400> 154
Met Asp Phe Met Leu Arg Tyr Met Tyr Asn Gln Glu Ser Val Asp Trp
                                   10
Val Gly Asp Tyr Asn Glu Pro Leu Thr Gly Phe Ser Trp Arg Gly Gly
Ser Glu Arg Glu Thr Thr Gly Ile Gln Ile Trp Ser Glu Ile Phe Leu
                            40
Ile Asn Lys Pro Asp Gly Lys Lys Val Ala Val Leu Leu Met Asp Thr
                        55
Gln Gly Thr Phe Asp Ser Gln Ser Thr Leu Arg Asp Ser Ala Thr Val
 65
                    70
                                       7.5
Phe Ala Leu Ser Thr Met Ile Ser Ser Ile Gln Val Tyr Asn Leu Ser
Gln Asn Val Gln Glu Asp Asp Leu Gln His Leu Gln Leu Phe Thr Glu
           100
                              105
Tyr Gly Arg Leu Ala Met Glu Glu Thr Phe Leu Lys Pro Phe Gln Ser
                           120
Leu Ile Phe Leu Val Arg Asp Trp Ser Phe Pro Tyr Glu Phe Ser Tyr
                       135
                                          140
Gly Ala Asp Gly Gly Ala Lys Phe Leu Glu Lys Arg Leu Lys Val Ser
                   150
                                      155
Gly Asn Gln His Glu Glu Leu Gln Asn Val Arg Lys His Ile His Ser
                                  170
Cys Phe Thr Asn Ile Ser Cys Phe Leu Leu Pro His Pro Gly Leu Lys
```

185

180

Val Ala Thr Asn Pro Asn Phe Asp Gly Lys Leu Lys Glu Ile Asp Asp 195 200 205

- Glu Phe Ile Lys Asn Leu Lys Ile Leu Ile Pro Trp Leu Leu Ser Pro 210 215 220
- Glu Ser Leu Asp Ile Lys Glu Ile Asn Gly Asn Lys Ile Thr Cys Arg 225 230 235 240
- Gly Leu Val Glu Tyr Phe Lys Ala Tyr Ile Lys Ile Tyr Gln Gly Glu 245 250 255
- Glu Leu Pro His Pro Lys Ser Met Leu Gln Ala Thr Ala Glu Ala Asn 260 265 270
- Asn Leu Ala Ala Val Ala Thr Ala Lys Asp Thr Tyr Asn Lys Lys Met 275 280 285
- Glu Glu Ile Cys Gly Gly Asp Lys Pro Phe Leu Ala Pro Asn Asp Leu 290 295 300
- Gln Thr Lys His Leu Gln Leu Lys Glu Glu Ser Val Lys Leu Phe Arg 305 310 315 320
- Gly Val Lys Lys Met Gly Gly Glu Glu Phe Ser Arg Arg Tyr Leu Gln 325 330 335
- Gln Leu Glu Ser Glu Ile Asp Glu Leu Tyr Ile Gln Tyr Ile Lys His 340 345 350
- Asn Asp Ser Lys Asn Ile Phe His Ala Ala Arg Thr Pro Ala Thr Leu 355 360 365
- Phe Val Val Ile Phe Ile Thr Tyr Val Ile Ala Gly Val Thr Gly Phe 370 380
- Ile Gly Leu Asp Ile Ile Ala Ser Leu Cys Asn Met Ile Met Gly Leu 385 390 395 400
- Thr Leu Ile Thr Leu Cys Thr Trp Ala Tyr Ile Arg Tyr Ser Gly Glu
  405 410 415
- Tyr Arg Glu Leu Gly Ala Val Ile Asp Gln Val Ala Ala Ala Leu Trp 420 425 430
- Asp Gln Gly Ser Thr Asn Glu Ala Leu Tyr Lys Leu Tyr Ser Ala Ala 435  $\phantom{\bigg|}440\phantom{\bigg|}445\phantom{\bigg|}$
- Ala Thr His Arg His Leu Tyr His Gln Ala Phe Pro Thr Pro Lys Ser 450 455 460
- Glu Ser Thr Glu Gln Ser Glu Lys Lys Lys Met
  465 470 475

# INTERNATIONAL SEARCH REPORT

International application No. PCT/US99/\$1005

	SSIFICATION OF SUBJECT MATTER		
` '	:C12N 15/00; C07K 1+/00 :+35/69.1; 536/23.5; 530/350		
	to International Patent Classification (IPC) or to bo	th national classification and IPC	
B. FIEL	DS SEARCHED		
Minimum d	ocumentation searched (classification system follow	ed by classification symbols)	
U.S. :	+35/69.1; 536/23.5; 530/350		
Documental searched	ion searched other than minimum documentation	to the extent that such documents are	included in the fields
	lata base consulted during the international search	(name of data base and, where practicabl	e, search terms used)
c. Doc	UMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where a	ppropriate, of the relevant passages	Relevant to claim No.
X	WO 97/39123 A2 (GENETICS INSTA 1997, page 87, SEQ ID No:23.	ITUTE, INC.) 23 OCTOBER	1-3, 5, 7
X	Database on EST, AN AA430259, HI EST Project 1997, sequence listing, document.		1-3, 5, 7
X, P	WO 99/00405 A1 (GENETICS INS 1999, page 47, SEQ ID No:2 at posit	•	1-3, 5-7
X	Database on Genbank, AN AB018272, NAGASE et al., 'Prediction of the coding sequences of unidentified human genes. XI. The complete sequences of 100 new cDNA clones from brain which code for large proteins in vitro,' sequence listing, DNA Res., 1998, 5(5), pages 277-286, see entire document.		1-3, 5, 7
Further documents are listed in the continuation of Box C.		C. See patent family annex.	
Special categories of cited documents:  T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory anderlying the invention			lication but cited to understand
To be of particular relevance  "E" earlier document published on or after the international filing date  "L" document which may throw doubts on priority claim(s) or which is  cited to establish the publication date of another citation or other		"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone	
special reason (as specified)  Odocument of particular relevance; the claimed invention of the considered to involve an inventive step when the document of particular relevance; the claimed invention of the considered to involve an inventive step when the document of particular relevance; the claimed invention of the considered to involve an inventive step when the document of particular relevance; the claimed invention of the considered to involve an inventive step when the document of particular relevance; the claimed invention of the considered to involve an inventive step when the document of particular relevance; the claimed invention of the considered to involve an inventive step when the document of particular relevance; the claimed invention of the considered to involve an inventive step when the document of particular relevance; the claimed invention of the considered to involve an inventive step when the document of particular relevance; the claimed invention of the considered to involve an inventive step when the document of particular relevance; the claimed invention of the considered to involve an inventive step when the document of the considered to involve an inventive step when the document of the considered to involve an inventive step when the document of the considered to involve an inventive step when the document of the considered to involve and inventive step when the document of the considered to involve an inventive step when the document of the considered to involve an inventive step when the document of the considered to involve an inventive step when the document of the considered to involve an inventive step when the document of the considered to involve an inventive step when the considered to involve an inventive step when the considered to involve an inventive step when the considered to involve and invo		when the document is combined	
"P" document published prior to the international filing date but later "2" document member of the same patent family than the priority date claimed			
<del></del>		Date of mailing of the international search report 17 APR. 2000	
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT		Authorized officer  ELIANE LAZAR-WESLEY	
Washington, D.C. 20231 Facsimile No. (703) 305-3230		Telephone No. (703) 308-0196	
orm PCT/ISA/210 (second sheet)(July 1992)*			

# INTERNATIONAL SEARCH REPORT

International application No. PCT/US99/51005

Box 1 Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)			
This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:			
Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:			
2. Claims Nos.:  because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:			
Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).			
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)			
This International Searching Authority found multiple inventions in this international application, as follows:			
Please See Extra Sheet.			
As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.			
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.			
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:			
+ X No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:			
Remark on Protest The additional search fees were accompanied by the applicant's protest.			
No protest accompanied the payment of additional search fees.			

Form PCT/ISA/210 (continuation of first sheet(1))(July 1992)\*

#### INTERNATIONAL SEARCH REPORT

International application No. PCT/US99/\$1005

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claims 1-7, drawn to an isolated protein of SEQ ID No:2 encoded by the polynucleotide of SEQ ID No:1, a polynucleotide sequence encoding the full length protein encoded by the cDNA insert of clone AK296\_li, and a composition.

Group II, claims 8-9, drawn to an isolated protein of SEQ ID No:22 encoded by the polynucleotide of SEQ ID No:21, and a polynucleotide sequence encoding the full length protein encoded by the cDNA insert of clone ASS+1i.

The inventions listed as Groups I-II do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the special technical teature of Group I is the polypeptide of SEQ ID No:2 and the polynucleotide of SEQ ID No:1. The polypeptide of SEQ ID No:22 and polynucleotide of SEQ ID No:21 of Group II do not share the special technical feature of Group I, as they have different structures and functions.